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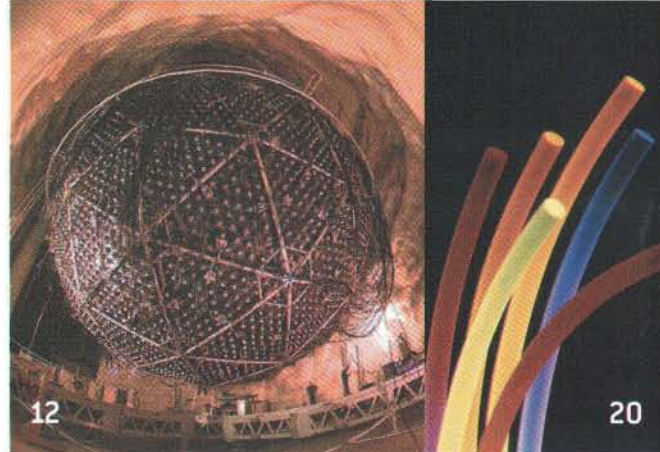
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ABOUT THE PHOTOGRAPHER: The work of Felice Frankel appears throughout this issue. Collaborating with scientists, Frankel creates film and digital imagery related to diverse areas of science, including nanotechnology. Her images have appeared in major national magazines and technical journals. In January 2002 the MIT Press will publish her guide to photographing science. Recently she received a three-year grant from the Alfred P. Sloan Foundation to co-author a book on nanotechnology with Harvard University's George M. Whitesides. She and Whitesides wrote a previous book, *On the Surface of Things: Images of the Extraordinary in Science* (Chronicle Books, 1997).

Cover image and preceding page: Felice Frankel, with technical help from J. Christopher Love; this page, clockwise from top left: Lawrence Berkeley National Laboratory; Robert Young Pelton/Corbis; Felice Frankel, with technical help from K. F. Jensen, M. G. Bawendi, C. Murray, C. Kagan, B. Dabbousi and J. Rodriguez-Viego of M.I.T.

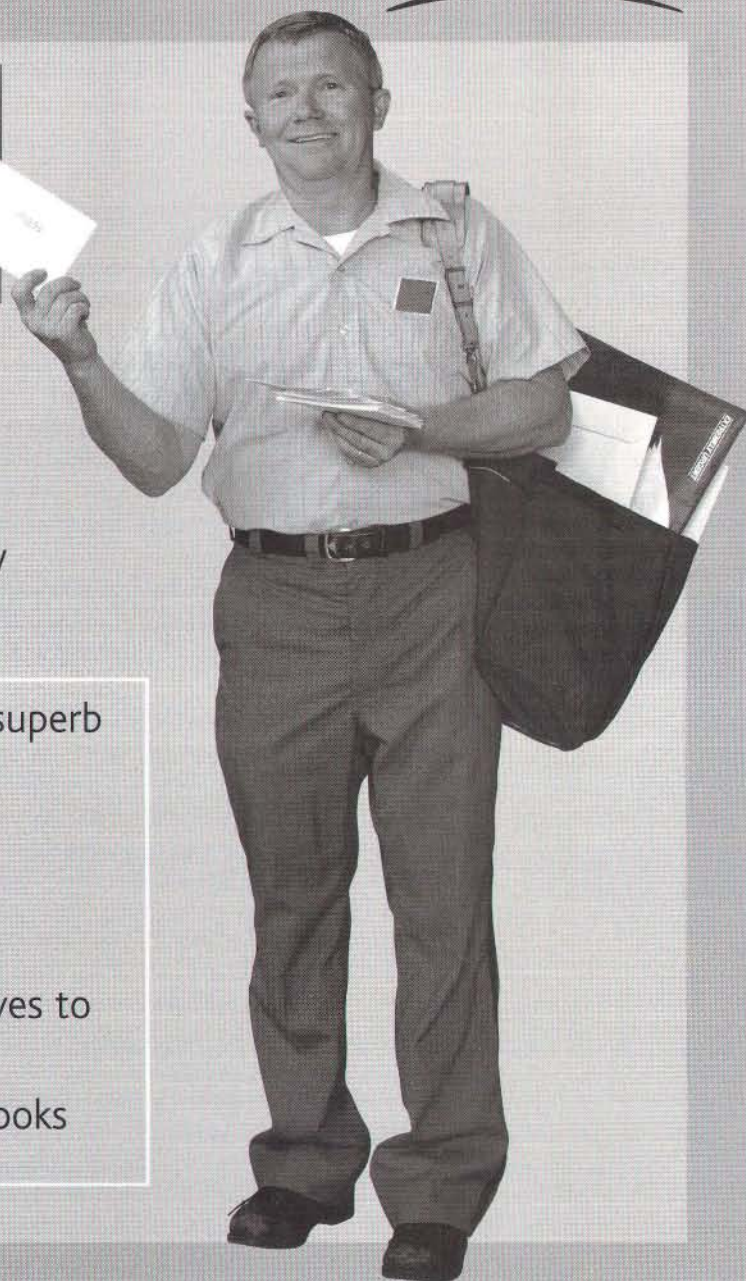


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Megabucks for Nanotech

Biologists sometimes stand accused of physics envy: a yearning for irreducible, quantifiable laws sufficient to explain the complex workings of life. But the jealousy goes both ways. Physicists, chemists and other nonbiologists have long suffered from what can only be called NIH envy: the longing for the hefty increases in research funding that seem to go every year to the National Institutes of Health.

From 1970 through 2000, federal backing for the life sciences more than tripled in constant dollars, whereas money for the physical sciences and engineering has by comparison remained flat. But last year the Clinton administration delivered a valentine to the physics, chemistry and materials science communities: the National Nanotechnology Initiative provided a big boost in funding for the science and engineering of the small. The initiative, moreover, seems to have staying power. The Bush

White House has targeted a more modest but still substantial increase for nanotech. If the president's budget request passes, federal funding for nanotechnology, at \$519 million, will have nearly doubled in the past two years, more than quadrupling since 1997.

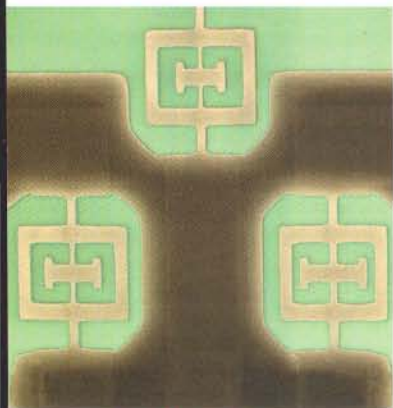
The initiative may prove to be one of the most brilliant coups in the marketing of basic research since the announcement, in 1971, of the "War on Cancer." Nanotechnology—the study and manufacture of structures and devices with dimensions about the size of a molecule—offers a very broad stage on which the research community can play. Nanometer-scale physics and chemistry might lead directly to the smallest and

fastest transistors or the strongest and lightest materials ever made. But even if the program gives special emphasis to the physical sciences and engineering, it has something for everyone. Biologists, of course, have their own claim on the molecular realm. And nanotechnology could supply instrumentation to speed gene sequencing and chemical agents to detect tumors that are only a few cells in size.

Of course, a program that tries to accommodate everyone could end up as a bottomless money sink. In his new book *Science, Money and Politics* (reviewed in this issue on page 88), journalist Daniel S. Greenberg warns of the dangers inherent in an indiscriminate, all-encompassing approach to research that eats up money. Skeptics have wondered whether sizable increases are warranted for such a nascent field. A Congressional Research Service report last year raised questions about why nanotechnology merited such generosity, given that some of its research objectives may not be achievable for up to 20 years.

But the initiative is more than mere marketing. A portfolio of diverse ideas—unlike a program focused on, say, high-temperature superconductivity—may help ensure success of a long-term agenda. The variety of research pursuits increases the likelihood that some of these projects will actually survive and flourish. Industry, in contrast, is generally reluctant to invest in broad-based research programs that may not bear fruit for decades.

Because the development of tools and techniques for characterizing and building nanostructures may have far-reaching applicability across all sciences, nanotechnology—the focus of this issue of *Scientific American*—could serve as a rallying point for physicists, chemists and biologists. As such, it could become a model for dousing NIH envy and the myriad other skirmishes that occur in the yearly grab for research dollars.



NANOMACHINES

THE EDITORS editors@sciam.com

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GEORGE STEINMEYER

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I On the Web

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THE SCIENTIFIC REASON TO GO ONLINE

FEATURED STORY

Looking for Aliens



We often assume that extraterrestrials possess the intelligence and the technology to contact us. But what if they aren't that smart? How would we find them? In fact, many scientists are now suggesting that when we discover alien life—if we do—it won't resemble the cunning eight-eyed rivals of *Star Trek* episodes. Instead, they say, it will most likely come in the form of tiny microbes. With that in mind, scientists at NASA's Jet Propulsion Laboratory are now developing ways to search for cells among the stars.

www.sciam.com/explorations/2001/071601alien/

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Letters

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WRITES FORMER PRESIDENT JIMMY CARTER, "I read with great interest 'The Arctic Oil & Wildlife Refuge,' by W. Wayt Gibbs. I had the privilege of signing the 1980 Alaska National Interest Lands Conservation Act, which established the Arctic National Wildlife Refuge and specifically prohibited oil development in its 1.5-million-acre coastal plain. I also had the opportunity to visit the area and witness its great herds of caribou, muskoxen and other wildlife. I feel that those in Congress who soon will render their own judgment on whether to protect or drill the Arctic refuge would benefit from reading your article."

For further comments on this and other articles from the May issue, please read on.



YOUR OIL OR YOUR WILDLIFE?

Those who refer to the Arctic National Wildlife Refuge (ANWR) as the last pristine wilderness in America ["The Arctic Oil & Wildlife Refuge," by W. Wayt Gibbs] either are purposely misrepresenting the facts or have never visited the region.

In truth, it is 100 miles of flat, barren, frozen tundra, a small part of the 1,100-mile coastline of Alaska on the Arctic Ocean. It is predicted to hold about the same quantity of oil as we have imported from Saudi Arabia during the past 30 years. It will keep the Alaska pipeline full for at least the next 30 years.

TED STEVENS

U.S. Senator, Alaska

The U.S. Geological Survey estimates that between six billion and 16 billion barrels of recoverable oil are in ANWR. Even if the mean estimate were discovered, it would be the largest oil field found worldwide in the past 40 years.

At a time when we face a significant energy crisis and our dependence on other nations for energy is rising, we must look here at home for solutions. Although ANWR alone is not the answer, we cannot ignore the tremendous resources that exist there. It can be safely explored and should be a part of our national energy strategy.

FRANK MURKOWSKI

U.S. Senator, Alaska

Chairman, U.S. Senate Energy and Natural Resources Committee

Gibbs noted the findings of several researchers who speculate that oil development and caribou cannot mix. But he failed to cite published, peer-reviewed scientific studies indicating that oil development in Alaska's Arctic has not affected calving success or herd growth. Any bill permitting oil development will require the highest degree of wildlife protection.

DON YOUNG

U.S. Congressman, Alaska

GIBBS REPLIES: According to the 2000 Annual Report of the U.S. Energy Information Administration, Saudi Arabia sent 10.7 billion barrels of oil to the U.S. from 1969 to 1999. That is half again as much as the best guess for the 30-year production from the 1002 Area. EIA analysts predict a maximum production rate from the refuge of about half a million barrels a day 10 years after development begins, with a peak of nearly a million barrels a day about a decade after that. To "keep the Alaska pipeline full" requires 2.1 million barrels a day, but only 1.1 million barrels flowed through it in 1999, and production is falling steadily. Alaska's Division of Oil and Gas estimates that 20 years from now North Slope oil fields outside of the 1002 Area will produce only 408,000 barrels a day.

There are large natural variations in the populations and breeding patterns of the animals that live on the North Slope, so any effect of human activities on those trends may not be visible until many years of data have been collected and many confounding factors have been studied and appropriately controlled for. Moreover, some of the studies that examined effects on caribou from North Slope oil devel-

opment are not immediately applicable to the 1002 Area because of differences in geography, herd size and the distribution of vegetation. Nevertheless, much of the older peer-reviewed research relevant to this debate was in fact cited in the article.

"The Arctic Oil & Wildlife Refuge" overstates the benefits of drilling by asking how much oil might ultimately be economically recovered if the cost of finding it were already sunk. But exploration costs—economic as well as environmental—also have to be considered when judging whether to allow drilling. If finding costs are included, then at a sustained West Coast price of \$24 a barrel (in 1996 dollars), the mean expected economically recoverable reserve is 5.2, not 7, billion barrels; at \$18, about 2.4, not 5, billion barrels; and at \$15, zero, not a few hundred million barrels. Both ways of considering recoverable reserves are legitimate, but I think the lower figure, counting finding costs, is the right one for the public policy decision.

AMORY B. LOVINS

Chief Executive Officer [Research]
Rocky Mountain Institute
Snowmass, Colo.

The question before us appears to be whether our rapacious appetite for oil will lead to the destruction of vast expanses of untouched wilderness, an irreplaceable sanctuary for polar bears, white wolves and caribou. For 20,000 years, the native Gwich'in people have inhabited this sacred place, following the caribou herd and leaving the awe-inspiring landscape just as they found it. For the sake of future generations, I hope the answer is no to drilling, despite advances in technology.

ROBERT REDFORD

Sundance, Utah

ALL ABOUT INKBLOTS

Scott O. Lilienfeld, James M. Wood and Howard N. Garb ["What's Wrong with This Picture?"] do not present a balanced analysis of the Rorschach; they overemphasize studies that do not support the

test's reliability and validity and ignore those that demonstrate its merits and sound psychometric properties.

They also fail to recognize that no psychological measure should be used in isolation when making clinical decisions. Well-trained Rorschachers know that interpretations based on any given test must be supplemented by information obtained through other methods. The Rorschach has prevailed because it captures the complexity of human functioning in a way that self-report measures alone do not.

LISA MERLO

DOUGLAS BARNETT

Department of Psychology
Wayne State University

LILIENFELD REPLIES: *Despite thousands of studies conducted on the Rorschach, only a handful of indices have received consistent empirical support. Merlo and Barnett are correct that the Rorschach should not be used in isolation when making clinical decisions, but they erroneously assume that adding the Rorschach to existing test information necessarily increases validity. In fact, in several studies validity decreased when clinicians with access to other test information were provided with Rorschach data.*

There is little evidence that Rorschach data contribute statistically to the assessment of personality or mental illness beyond questionnaire data. Although the Rorschach yields immensely detailed and complex data, we should not make the mistake of assuming that these data are necessarily valid or useful.

SEMANTIC WEB: NOT FUZZY

What struck me as a curious omission in "The Semantic Web," by Tim Berners-Lee, James Hendler and Ora Lassila, was any mention of the notion of fuzzy logic. Even today's relatively primitive search engines attempt to rate the relevance of hits to the supplied search terms.

ROB LEWIS

Langley, Wash.

BERNERS-LEE REPLIES: *I deliberately didn't mention fuzzy logic, as fuzzy logic itself does not work for the Web. I see fuzzy logic and oth-*

er heuristic systems as being used within agents that trawl the Semantic Web. I see the output of such systems as being very useful and sometimes so valuable that it is reentered into the Semantic Web as trusted data. But it can't be the basis for the Semantic Web. In the basic Semantic Web you have to be able to follow links successively across the globe without getting fuzzier.

E. COLI-FREE COOKOUTS

In "Antimicrobe Marinade" [Staking Claims], Gary Stix presents three new, high-tech methods to decrease *E. coli* 0157:H7 in meat. I, for one, plan on continuing to fall back on an older (Neanderthals used it), low-tech but foolproof method to kill the bacteria: cooking. If all the effort at developing high-tech means of control were redirected at educating everyone about known control methods—avoiding cross-contamination and cooking the inside of burgers to 160 degrees or higher ("cook the pink out")—the *E. coli* problem we have now might just go away.

WINKLER G. WEINBERG

Section Chief, Infectious Disease Service
Kaiser Permanente
Atlanta

SUPERCAVITATION, SWIMMINGLY

In reading "Warp Drive Underwater," by Steven Ashley, I tripped over the statement that "swimming laps entirely underwater is even more difficult" than swimming on the water's surface. Actually, it is much easier to swim several laps underwater with a single breath than it is to swim on the surface, because the air/water boundary friction is even greater than the water friction. In fact, competitive swimming rules for years stipulated that swimmers could not become entirely submerged during the breaststroke.

JON TOBEY

Monroe, Wash.

ERRATUM To determine how far you've driven, multiply [not divide, as was incorrectly stated in "Rip Van Twinkle," by Brian C. Chaboyer] the fuel supply by the gas mileage.

| 50, 100 & 150 Years Ago

Salmon Sense ■ Okapi Surprise ■ Yankee Ingenuity

SEPTEMBER 1951

HOW SALMON GET HOME—"An explanation of one of the most engaging phenomena of nature—the salmon's return from hundreds of miles at sea to its native creek—has been proposed by Arthur Hasler and Warren Wisby of the University of Wisconsin. They believe that the fish can smell its way back home. 'It appears that substances in the water, probably coming from the vegetation and soils in the area through which the stream runs, give each stream an odor which salmon can smell, remember and recognize even after a long period of non-exposure.' The damming of many Pacific Coast salmon streams is resulting in a progressive decline of the yearly catch, as huge numbers of salmon batter themselves to death trying to get over the dams and back home."

ENGINEERS—"In 1850 a little more than 5 per cent of America's industrial power was supplied by machines; 79 per cent was furnished by animals and 15 per cent by human muscles. Today 84 per cent of our power is supplied by machines and only 12 per cent by animals and 4 per cent by men. As a consequence the engineer has become an increasingly impor-

tant factor in our civilization. There are 400,000 of them in the U.S., and engineering is now our third-largest profession, exceeded only by teaching and nursing. However, engineers are in acutely short supply, and the number of graduates in the next few years will be far short of the need for new engineers."

SEPTEMBER 1901

OXYGEN FOR AERONAUTS—"An apparatus has been devised by a Frenchman, Louis-Paul Cailletet, for the purpose of supplying aeronauts with pure oxygen when poised at a high altitude, where the extreme rarefaction of the air renders them liable to asphyxiation. When the aeronauts experience the nausea arising from rarefied air, they have recourse to an oxygen supply. His device consists of a double glass bottle containing liquid oxygen. From the reservoir extends a flexible tube communicating with a small metal mask covered externally with velvet to protect it from the cold."

THE OKAPI DISCOVERED—"Sir Harry Johnston's discoveries in Uganda are of great importance. One of the new animals which he found was the 'Okapi.' It belongs to a group of ruminants represent-

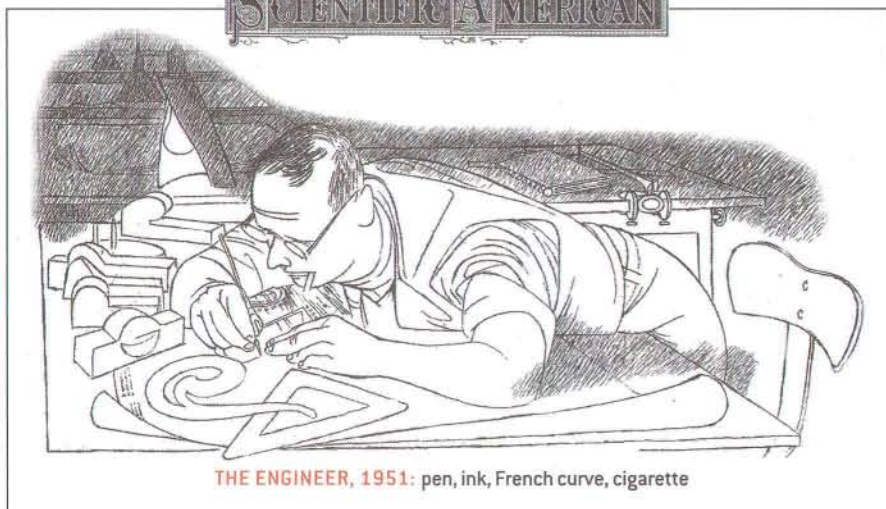
ed at the present time only by the giraffe and the prong-horned antelope, so-called, of North America. So far as it can be ascertained, the okapi is a living representative of the Hellatotherium genus, which is represented by an extinct form found fossilized in Greece and Asia Minor. The animal is about the size of a large ox. The coloration is, perhaps, unique among mammals. The body is of a reddish color, the hair is short and extremely glossy. Only the legs and hind quarter of the animal appear to be striped."

SEPTEMBER 1851

MECHANICAL REAPER—"The *Illustrated News*, London, says: 'McCormick's reaping machine had a fair trial, at the annual gathering at Mechi's farm. It rained in torrents, and mud and wet straw soon clogged the other instruments; but we have the authority of, among others, Mr. Fisher Hobbes, the well-known agriculturalist, for stating that McCormick's machine performed its work perfectly, and proved itself one of the most valuable agricultural inventions of the age. It has arrived at the fortunate period, when the steady emigration of Irish laborers threatens to leave our farmers short of hands at every harvest. The proprietor will be ready to bear witness that he found no impediments from British jealousy, and that his success was hailed with as much enthusiasm as the damp weather would allow.'"
[Editors' note: Cyrus McCormick is considered to be the inventor of the first successful mechanical reaping machine.]

OUR EARLY YEARS—"From small beginnings, six years ago, the *Scientific American* has attained a very honorable position in point of circulation, and consequent influence and usefulness. No man can spend two dollars to better advantage than by subscribing for it. We may confidently expect over 20,000 patrons to our new volume. The more we have to feed, the better fare we will serve you."

SCIENTIFIC AMERICAN



THE ENGINEER, 1951: pen, ink, French curve, cigarette

SNO Nus Is Good News

THE LATEST ON MUTATING NEUTRINOS SOLVES THE SOLAR NEUTRINO PROBLEM BY GRAHAM P. COLLINS

Telltale flashes of light within a 1,000-ton sphere of ultrapure heavy water, deep underground in a nickel mine near Sudbury, Ontario, have resolved a 33-year-old puzzle. In June the Sudbury Neutrino Observatory (SNO) collaboration announced firm evidence that elusive ghostly particles called neutrinos morph from one subspecies to another during their flight from the sun to Earth. The result reassures astrophysicists that their precision solar models do not contain a lurking blunder, and it gives particle physicists further clues to what lies beyond their beloved but incomplete Standard Model of particle physics.

The mystery of solar neutrinos has haunted physicists since 1968, when the first experiment to count those neutrinos came up with less than half of the expected number. Three decades of experiments and more refined theories

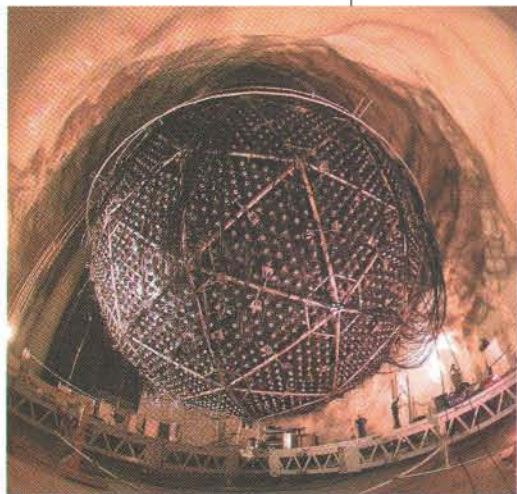
have only confirmed the discrepancy.

The SNO project is unique in that it uses heavy water, containing the deuterium isotope of hydrogen, to observe neutrinos (denoted by the Greek letter "nu"). A similar detector, Super-Kamiokande in Kamioka, Japan,

has been counting neutrinos in ordinary water for about five years. As Super-K member Edward Kearns of Boston University explains, "Although SNO is 10 times smaller, because the deuterium reaction is pretty strong, it has a comparable total event rate as Super-Kamiokande."

More important than the gross numbers, however, is the variety of interactions possible at SNO, giving the detector new ways to distinguish subspecies, or flavors, of solar neutrinos. In both heavy and ordinary water, a neutrino can hit an electron, sending it careering through the liquid fast enough to produce a flash of Cherenkov radiation. But such electron scattering can be caused by any of the three neutrino flavors: the tau-neutrino, the muon-neutrino and the electron-neutrino. (The sun's nuclear reactions produce electron-neutrinos exclusively.) SNO's heavy water can single out electron-neutrinos, because that flavor alone can be absorbed by a deuterium nucleus, transforming it into two protons and an electron that fly apart at high energy.

SNO's count of just the electron-neutrinos is lower than Super-K's count of all flavors. The conclusion: some of the sun's electron-neutrinos turn into muon- or tau-neutrinos. Because muon- and tau-neutrinos scatter electrons much less efficiently than electron-neutrinos do, the small excess of scatterings at Super-K translates into a large number of muon-



TO SEE NEUTRINOS from the sun, the underground Sudbury Neutrino Observatory (SNO), shown here during construction, relies on 9,456 sensors to monitor a 1,000-ton sphere of water. Physicists use the Greek letter "nu" to denote neutrinos.

TO COME:
MORE NU NEWS

In the next few months
SNO researchers will:

- Determine whether the amount of solar neutrino oscillation varies according to the time of day and the season. Such variations, not discerned at Super-Kamiokande, would result from extra oscillations when neutrinos pass through Earth or because of Earth's varying distance from the sun.
- See if the oscillation depends on the neutrinos' energy. The data will further constrain the neutrino masses and the so-called mixing angle (which defines how much oscillation can occur) and might eliminate some oscillation theories.

or tau-neutrinos present. Two thirds of the electron-neutrinos from the sun are transformed by the time they reach Earth—precisely the right number to agree with the predictions made using solar models. Arthur B. McDonald, head of the SNO project, says that the result “provides a very good confirmation that we understand how the sun is generating energy with great accuracy.”

Changes, or oscillations, of neutrino flavors can occur only between flavors having unequal masses. In essence, a subtle mass difference causes the quantum waves of two different flavors to oscillate in and out of sync with each other, like two close musical notes producing beats. If the peak of each beat corresponds to an electron-neutrino, then the minimum in each cycle is, say, a muon-neutrino. The first strong evidence for such oscillations came in 1998 from Super-K's study of high-energy cosmic-ray neutrinos.

In the simplest version of the Standard Model of particle physics, neutrinos are massless and cannot oscillate. Most theorists view

neutrino masses as something to be explained by whichever theory supersedes the Standard Model. The masses are tiny: the SNO results, combined with other data, imply that all three neutrino flavors have masses less than $1/180,000$ of an electron mass, the next heavier particle.

SNO's results put sterile neutrinos—a peculiar hypothetical fourth flavor—on shakier ground. All the observed SNO and Super-K data can be explained by electron-muon-tau oscillations. Contributions by sterile neutrinos are not yet ruled out, “but the fraction of sterile neutrinos is not expected to be large,” McDonald says.

The SNO experiment will continue for a few more years. Since June the detector has been running with ultrapure salt (sodium chloride) added to the heavy water. The chlorine atoms in the salt greatly enhance the detection of neutrons, produced when neutrinos split a deuterium nucleus without being absorbed. Accurate counts of those reactions should be a recipe for further tasty results about neutrinos.

ONCOLOGY

Cancer in the Crosshairs

WHY SOME TUMORS WITHSTAND GLEEVEC'S TARGETED ASSAULT BY DIANE MARTINDALE

Approved for use this past May, Gleevec was celebrated as the first in a wave of supremely effective cancer drugs that home in on tumors without harming healthy cells. In clinical trials, 90 percent of patients in early stages of chronic myelogenous leukemia (CML), a rare blood cancer, went into remission within six months of first taking Gleevec. Despite its promise, however, Gleevec and drugs like it may be only a provisional measure. More recent reports have found that patients in late-stage CML relapse because their tumors become drug-resistant.

Gleevec, made by Novartis, belongs to a class of drugs called small molecules. They are designed to either target specific receptors on cancer cells or disrupt their signaling pathways, thereby marking a major departure from radiation and chemotherapy, the broad effects of which can be toxic to healthy cells.

CML is caused when chromosomes 9 and 22 swap genes. This produces a mutation in the Abl protein, a type of internal signaling enzyme known as a tyrosine kinase that is involved in normal cell growth. Once mutated, however, the Abl protein becomes hyperactive and drives white blood cells to divide incessantly. In either form, Abl needs to bind a molecule of a cell's ATP to function. Gleevec works by docking into the pocket ordinarily occupied by ATP, thereby stopping the function of the signaling protein. The CML cells then pack up and die.

But why are CML cells the only ones killed, given that there are hundreds of other tyrosine kinases and similar enzymes that rely on ATP for their activation? Why doesn't Gleevec block these? Years ago scientists believed that all ATP binding sites were identical. Actually, they are all slightly different,



REASON TO SMILE: Gleevec's pioneer Brian Druker at a May press conference announcing the cancer drug's approval.

SMALL MOLECULES'
BIG BROTHER

Small-molecule drugs such as Gleevec are not the only targeted therapy. Another is **monoclonal antibodies**, which are created from a single cell and are designed to respond to a specific antigen. In cancer therapy, most block growth factors from activating cell division. For example, the monoclonal antibody Herceptin targets an epidermal growth factor on certain types of breast cancer cells. Although early results are encouraging, monoclonal antibodies are not nearly as impressive as Gleevec. Moreover, antibodies will bind to the same receptors on normal cells, thereby causing more severe side effects.

says Brian J. Druker, a cancer researcher at Oregon Health Sciences University who helped to develop Gleevec: "This was unpredicted, but good for the targeted approach."

Moreover, such molecules strike a blow at tumor cells' weak spot: their almost exclusive dependence on the mutated protein. Blocking the errant Abl cuts off the tumor cells' lifeline, but normal cells are unaffected because they possess redundancy in protein function; their backup pathways kick in, Druker explains.

The targeted approach offers much hope—Gleevec also blocks protein receptors in two other malignancies—but it is no magic bullet, warns Tony Hunter, a molecular biologist at the Salk Institute for Biological Studies in San Diego. Gleevec has been used for a short time (its approval came after clinical trials that began in 1998), and some patients have already developed resistance to it—the Abl protein's ATP pocket mutates so the drug can no longer bind to it. In other instances, production of the Abl protein is so great that the drug—even at the highest dose—cannot keep up. "Cancer

cells are genetically malleable," Hunter notes, "and they find ways to escape, no matter how clever we think we've been."

Small-molecule therapy is being viewed as a treatment, not a cure, Hunter adds. In some patients, particularly those in advanced stages of disease, the drugs may work only to keep the tumor in check, transforming it into a chronic condition, much as diabetes is.

Still, Gleevec is a milestone not just for what it does but for the revolutionary strategy it represents, says Larry Norton, head of solid-tumor oncology at Memorial Sloan-Kettering Cancer Center in New York City. He predicts that because of the new understanding of tumors at the molecular level, cancers will soon be classified by their molecular makeup rather than by their location in the body, as is done today. Researchers might then build molecules to attack them—a tall order, Norton says, "but one that is possible."

Diane Martindale is a science writer based in New York City.

GEOSCIENCE

Triggering a Snowball

DID METHANE ADDICTION SET OFF EARTH'S GREATEST ICE AGES? BY SARAH SIMPSON

EDINBURGH, SCOTLAND—Once upon a time ice as much as a kilometer thick engulfed the earth. Glaciers scoured the nearly lifeless continents, and sea ice encapsulated the oceans—even in the tropics. The planet's only solution to the deep freeze was to wait for volcanoes to release enough heat-trapping carbon dioxide to create a runaway greenhouse effect. A brutal episode of warming ensued, not only melting the ice but also baking the planet.

Three years ago a group of Harvard University researchers proposed this revolutionary idea—dubbed the snowball earth hypothesis—about the potential of the planet for severe climate reversals. Since then, scientists have

hotly debated the details of the events, which occurred as many as four times between 750 million and 580 million years ago, in a time known as the Neoproterozoic. But just how the earth first plunged into a snowball-style ice age has been unknown. Now the original purveyors of the snowball earth hypothesis have proposed a trigger: methane addiction.

At a scientific conference in Edinburgh this past June, geochemist Daniel P. Schrag described the addiction scenario: Just before the first snowball episode, the ancient earth kept warm by relying on methane—a greenhouse gas 60 times more powerful than carbon dioxide. The methane had begun leaking slowly into the atmosphere when massive, icy methane hydrate deposits within the seafloor became destabilized somehow. As a result, carbon dioxide levels decreased, and methane became the world's dominant greenhouse gas.

The trouble with the planet's dependence on methane is that the gas disappears quickly



MASSIVE GLACIERS entombed the earth hundreds of millions of years ago, but how?

in an oxygen-rich atmosphere. An interruption in the methane leak left the earth in dire need of greenhouse gases, and the climate tumbled into a deep freeze before volcanoes could release enough carbon dioxide to make up for the lost methane. "I'm not sure I totally buy this idea—it's outrageous," Schrag admitted at the conclusion of his presentation. "But it's the only idea that explains the carbon isotope crash just before the glaciations."

Such bizarre drops in carbon isotope values have been recorded in the rocks beneath the jumbled layers deposited by the glaciers of snowball events at several locations around the world. But as provocative as the methane addiction hypothesis may be, it left the conference audience with many questions.

Alan Jay Kaufman, a University of Maryland geochemist who first measured some of the carbon isotope crashes, pointed out that a dramatic decrease in biological productivity

in the oceans can also cause carbon isotope values to fall and remain low over periods of a million years or so. But based on estimates of sedimentation rates of the rocks in question, Schrag and others think the crash could have occurred over a shorter time frame. Still, Kaufman is skeptical: "We don't have any way to look into the rock record and see a methane buildup."

"It's difficult to test anything that old," Schrag says. But you can look for carbon isotope crashes in places where their duration may be more certain, he adds. Several workers have already correlated the carbon isotope values among Neoproterozoic rocks in Namibia, Australia, California, Canada and the Arctic islands of Svalbard. Dozens of other deposits of similar age exist but have not yet been analyzed. The potential triggers of a snowball earth, it seems, may be as controversial as the details of the event itself.

THE DISTANT PAST'S ELUSIVE CLUES

Information about the chemical makeup of the ancient atmosphere can sometimes be gleaned from the remains of bacteria trapped in rocks. If the number of fossilized methane-loving bacteria is unusually high, for instance, scientists can reasonably assume that the atmosphere was rich in that particular gas. But rocks from snowball earth times have experienced the heat and pressure of metamorphism, which have long since destroyed any biological cells.

CONSERVATION

Into the Jaguar's Den

HUNTING AS A MEANS TO PRESERVE THE JUNGLE'S FOREMOST PREDATOR BY ERIC NIILER

CAOBAS, MEXICO—Hunting jaguars is all about keeping your head low while running through the jungle—the better to duck spike-covered vines and saw-toothed palm leaves that infest this remote area of Mexico's Quintana Roo state in the Yucatán Peninsula. It's a several-million-acre patchwork of rain forest between two protected national parks that is rapidly being cut down by farmers, ranchers and small-scale loggers. As the forest goes, so does habitat for this region's most charismatic animal: *Panthera onca*, known locally as *el tigre*.

Catching the nocturnal jaguars means entering the jungle in the early hours before dawn; otherwise, heat and sunlight evaporate the cat's scent trail. After alternately running and stumbling for two hours, the hunting party stops and listens to the sound of barking dogs. "They've treed him," concludes Tony Rivera, who is leading us. "That's it!" Two trackers with machetes run ahead.

Soon we see a female jaguar, weighing

perhaps 70 pounds, nestled 30 feet above the forest floor. It gazes impassively at us with huge brown-yellow eyes. The jaguar's beautiful golden, black-spotted fur keeps it well hidden in the forest canopy. Mayan kings wore

TAKEN DOWN: Wildlife veterinarian Marcela Araiza checks a darted jaguar's health and genetic information.



jaguar skins as battle tunics; modern-day poachers prize them as proof of vanquishing the jungle's most powerful predator.

Joe Bojalad, a big-game hunter, rests for a minute and squints through the rifle scope. Hunters like him have paid upward of \$5,000 for this opportunity. He steadies the rifle, pulls the trigger and *ppffft*—the shot misses. “It didn’t go in?” he asks. In this case, big-game hunting does not mean killing. Bojalad has an air-powered rifle that fires tranquilizer darts. Once asleep, the jaguar will be examined and tagged.

Scientists don’t know exactly how many jaguars survive in the tropical forests of Latin America. The cats once flourished from the southern U.S. all the way to Argentina. Today only a few significant populations remain, mostly in Mexico, Belize and Brazil. Dart hunting is part of a unique program sponsored by *Unidos para la Conservación*, a Mexico City-based conservation group, the National Autonomous University of

warthogs and other game are targeted, some conservationists have complained that animals often get darted more than once, potentially resulting in tranquilizer poisoning, and that partial injections from poor shots merely frighten animals and could lead them to injure themselves. As for the jaguars, Alan Rabinowitz, director of the New York City-based Wildlife Conservation Society’s Global Carnivore Program, claims that science isn’t the top priority. “The project is being driven from a hunting perspective,” says Rabinowitz, who has visited the Mexican project. “Don’t tell me it’s a scientific project.”

The jaguar project’s principal investigator, UNAM’s Gerardo Ceballos Gonzales, defends the program. He says that its early problems with U.S. hunters—their wish to shoot already collared animals, for example—have been corrected with stricter protocols.

According to Ceballos, the project plans to capture eight to 10 jaguars inside the nearby Calakmul Biosphere Reserve and another 10 in the mixed forest and farming country around it in the next year. Close to 20 animals have been collared since the project began; the team is currently tracking five animals.

Once the collaring program is completed, Ceballos plans to set up a network of motion-detecting cameras across trails. These cameras will record both predator and prey and will help determine the size of the jaguar population, now estimated at 400 to 500 within the reserve. Outside Brazil’s Pantanal region, this may be the world’s largest jaguar population. “The hope is that we can have a sustainable population of jaguars not only inside but outside the reserve,” Ceballos remarks.

Yet Rabinowitz and others also worry about the presence of guides such as the 50-year-old Rivera, a former poacher. In the late 1980s Rivera ran afoul of the U.S. Fish and Wildlife Service for transporting jaguar skins into the U.S. Rivera says he’s changed his spots and no longer kills jaguars, although he believes there are enough jaguars in this part of Mexico to sustain limited hunting.

The problem here is not illegal hunting or the possibility of its return but rather deforestation, according to Carlos Manterola, director of *Unidos para la Conservación*. Manterola recently began working with local community landowners to start a mahogany-furniture workshop that will boost the value



YUCATÁN FORESTS harbor one of the few remaining populations of jaguars.

WHEN ANIMALS ARE EASY PICKINGS

One of the controversial aspects of the dart hunting of jaguars is the use of live bait: **goats are tied up at night to entice the predator**, à la *Jurassic Park*, says Marcelo Aranda, a biologist at Mexico’s Ecology Institute in Veracruz. Perhaps as a result of the practice, one jaguar that was collared and released in April was caught at a nearby farm in late May after it had killed four sheep, a cow and a young calf. The 150-pound male was relocated to the Sian Ka’an Biosphere Reserve, about 100 miles away. Project defenders say that the problem jaguar was an anomaly—so far none of the other collared jags has attacked livestock.

Mexico (UNAM), and Safari Club International, a U.S.-based outfit that recruits American big-game hunters to fund conservation and research. A Mexican cement company and a cellular-phone firm donate additional funds to the project, which has been run by *Unidos para la Conservación* since 1997.

Twice again, Bojalad fires. But no luck. The gun is passed to one of the trackers, who shimmies up a nearby tree to get a better angle, takes aim and nails the jaguar. Disoriented by the ketamine tranquilizer, the cat scrambles down the tree and stumbles through the jungle with three dogs at its heels before plopping over.

For the next 45 minutes, Cuauhtemoc Chavez, a graduate student from Mexico City, and Marcela Araiza, a wildlife veterinarian, take skin, muscle and blood samples. They remove more than 30 botfly larvae that have burrowed into the animal’s hide and then attach a GPS radio collar. Over the next year and a half, the collar will record the animal’s location.

Not everyone is convinced that dart hunting is a good idea. In Africa, where rhinos,

of the region's timber and perhaps slow its cutting. He also pays local farmers if the jaguars eat livestock, an insurance policy designed to cut poaching. "This is not just a scientific project for jaguars," Manterola insists. "We are using the jaguar as a flagship species for conservation of the Mayan jungles."

Eric Nüller, based in San Diego, writes frequently about conservation issues.



TAKING AIM at a treed jaguar is Joe Bojalad; Tony Rivera (center) and Carlos Manterola (right) look on.

news
SCAN

PRIVACY

Surveillance by Design

WILL A NEW CYBERLAW BYPASS THE U.S. CONSTITUTION? BY WENDY M. GROSSMAN

LONDON—A legislative move in Europe that would also affect the U.S. is threatening the sometimes controversial ability of Internet users to mask their real-world identities. The move, which is heavily backed by the U.S. Department of Justice, is the cybercrime treaty, designed to make life easy for law enforcement by requiring Internet service providers (ISPs) to maintain logs of users' activities for up to seven years and to keep their networks tappable. The Council of Europe, a treaty-building body, announced its support of the cybercrime effort in June.

Anonymity is a two-edged sword. It does enable criminals to hide their activities. But it is also critical for legitimate citizens: whistleblowers, political activists, those pursuing alternative lifestyles, and entrepreneurs who want to acquire technical information without tipping off their competitors.

Even without the proposed legislation, anonymity is increasingly fragile on the Net. Corporations have sued for libel to force services to disclose the identities of those who posted disparaging comments about them online. Individual suits of this type are rarer, but last December, Samuel D. Graham, a former professor of urology at Emory University, won a libel judgment against a Yahoo user whose identity was released under subpoena.

Services designed to give users anonymity sprung up as early as 1993, when Julf Helsingius founded Finland's anon.penet.fi, which stripped e-mail and Usenet postings of identifying information and substituted a

pseudonymous ID. Users had to trust Helsingius. Many of today's services and software, such as the Dublin-based Hushmail and the Canadian company Zero Knowledge's Freedom software, keep no logs whatsoever.

But if the cybercrime treaty is ratified, will they still be able to? Would they have to move beyond the reach of the law to, say, Anguilla? More than that, will the First Amendment continue to protect us if anonymity is effectively illegal everywhere else? Says Mike Godwin, perhaps the leading legal specialist in civil liberties in cyberspace: "I think it becomes a lot harder for the U.S. to maintain protection if the cybercrime treaty passes." Godwin calls the attempt to pass the cybercrime treaty "policy laundering"—a way of using international agreements to bring in legislation that would almost certainly be struck down by U.S. courts. (On its Web site, the U.S. Department of Justice explains that no supporting domestic legislation would be required.)

In real-world terms, the equivalent of the treaty would be requiring valid return addresses on all postal mail, installing cameras in all phone booths and making all cash traceable. People would resist such a regime, but surveillance by design in the electronic world seems less unacceptable, perhaps because for some people e-mail still seems optional and the Internet is a mysterious, dark force that is inherently untrustworthy.

Because ISPs must keep those logs and that data, your associations would become an open book. "The modern generation of

FOR ME BUT NOT FOR YOU?

As counterculturalist Stewart Brand has said, **anonymity can be toxic to community**, because it can foster irresponsible activity and sow mistrust. But an experiment some years back on the WELL, the San Francisco-based electronic conferencing system, showed that people typically wanted anonymity for themselves—just not for others.

PRECEDENTS FOR PRIVACY

In the U.S., the right to be anonymous is protected under the First and Fourth amendments. According to Mike Godwin, author of *Cyber Rights*, two significant Supreme Court cases establish the precedents.

NAACP v. Alabama The 1958 ruling upheld the NAACP's refusal to disclose its membership lists on the grounds that this type of privacy is part of the right to freedom of assembly.

McIntyre v. Ohio Elections Commission The 1995 ruling struck down a requirement, instituted to control campaign spending, that political pamphlets include the name and address of their issuer.

traffic-analysis software not only can link to conventional police databases but can give a comprehensive picture of a person's lifestyle and communications profile," says Simon Davies, director of Privacy International. "It can automatically generate profiles of thousands of users in seconds and accurately calculate friendship trees."

In the not too distant future, nearly everything that is on hard copy today will travel via e-mail and the Web, from our medical records to the music we listen to and the books we

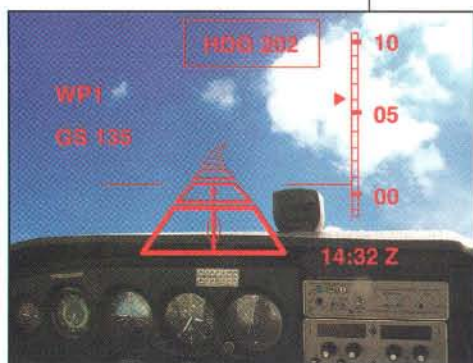
read. Whatever privacy regime we create now will almost certainly wind up controlling the bulk of our communications. Think carefully before you nod to the mantra commonly heard in Europe at the moment: "If you have nothing to hide, you have nothing to fear." Do you really want your medical records sent on the electronic equivalent of postcards?

Wendy M. Grossman, who writes about cyberspace issues from London, is also on the board of Privacy International.

DISPLAYS

Eye Spy

NOMAD PUTS TEXT AND GRAPHICS RIGHT ONTO THE RETINA BY PHIL SCOTT



PILOT'S-EYE VIEW using Nomad would show an overlaid flight path.

NEED TO KNOW: INSIDE VIEW

The heart of the Nomad technology lies in a microelectromechanical system (MEMS)—specifically, a MEMS light-beam scanner, which has a tiny mirror 1.5 millimeters wide. A red laser diode bounces a pulsed beam off the MEMS mirror, which uses an electromagnetic system to move in two directions, creating a scanning pattern similar to those on television screens. An optical combiner modifies the beam to create an image 800 pixels wide by 600 pixels long.

Matt Nichols, director of communications for Microvision, has just arrived from his crosstown walk. He's hurried from New York City's upcoming Museum of Sex, where he showed off the same equipment that he wants to demonstrate now. No, please—it's called Nomad, a retinal scanning device that can beam words and graphics directly into the viewer's eye. "They're trying to figure out how to create a fully interactive museum," Nichols sheepishly explains.

The U.S. Army is also interested in Nomad, for a less titillating function: equipping its helicopter pilots. When coupled with the proper software, the headset can display altitude, heading, speed, course and weapons status, all presented in a nice monochrome light beam that doesn't hamper the pilot's view. "It projects the image desired into the visual field of the pilot's eye, and that image is seen at optical infinity," says Thomas Lippert, chief scientist at Microvision, based in Bothell, Wash. "That means the pilot can keep his gaze out the windscreen while keeping this augmented information sharply in focus."

Such technology could replace head-up displays on windscreens and virtual-reality helmets—a goal of the U.S. Air Force for decades. Nomad is lightweight (the production version could weigh in at about one pound), and because it is worn, it will swivel

with the pilot's head. That makes it ideal for helicopters, which are inherently unstable and difficult to fly under instrument-only conditions. "It also means that in a heavy-vibration environment—the thump-thump-thumping of the rotors—the image remains stabilized in space," Lippert adds. "It doesn't bounce around like a bad newsreel." Other manufacturers have built head-mounted displays in the past, but Nomad superimposes images without blocking the view (the images are in outline form).

In late June the company conducted Nomad's first flight tests; eventually, Nichols states, the system will incorporate a voice-operated computer. Microvision intends to sell a commercial version as early as this fall for between \$8,000 and \$10,000.

Helicopter pilots aren't the only ones who might take advantage of the technology, Nichols adds. Air-traffic controllers could watch airplanes while their headsets broadcast the flight data. Surgeons might have a patient's medical images alongside real-time readouts of vital signs. Firefighters could enter smoke-filled buildings with overlaid room diagrams. The system has even allowed patients with macular degeneration to read once again. And of course, there's the Museum of Sex. But we'll let you fill in your own uses for the headset there.

Phil Scott is a science and technology writer in New York City.

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DATA POINTS:
A DEMON-HAUNTED
WORLD



Belief in some paranormal phenomena is on the rise in the U.S.

	Percent who believe	Percent change from 1990
Psychic or spiritual healing	54	+8
Extrasensory perception	50	+1
Haunted houses	42	+13
Ghosts or spirits	38	+13
Telepathy	36	0
Extraterrestrials have visited the earth	33	+6
Astrology	28	+3
Communication with the dead	28	+10
Reincarnation	25	+4

Percent change in the Nielsen ratings of *The X-Files* from its peak season: -29.8

SOURCES: Gallup Organization; Nielsen Media Research, 2000-01 season average compared with 1997-98 average. Psychic-healing category includes belief in the power of the mind to heal the body.

ASTRONOMY

Moons over Saturn

Saturn's family has gotten bigger. Researchers using 11 different telescopes around the world have reported finding 12 new moons, ranging from six to 32 kilometers in diameter and orbiting Saturn in highly eccentric paths, quite unlike the generally circular orbits of its major moons, such as Titan. These tiny moons seem to be clustered in groups of three or four, suggesting that they are remnants of larger bodies that were fractured, probably by collisions, early in the planet's formation. Such irregular bodies may be common for the gas giants; in the past few years astronomers have found five irregulars around Uranus and 12 around Jupiter. The latest finding, in the July 12 *Nature*, brings Saturn's satellite brood to 30: six major moons and 24 minor ones.

—Philip Yam



COMMUNICATIONS

Built for Speed

IBM attested in June to building the world's fastest silicon-based transistor. Potentially able to operate at 210 gigahertz, this silicon germanium transistor performs 80 percent faster than previous technology, breaking the 200-GHz speed barrier thought to exist for silicon-based transistors. Transistor speed depends largely on the distance electricity must travel within the device, and IBM researchers

were able to shrink this distance in so-called heterojunction bipolar transistors, in which electrons flow along a vertical path rather than taking the horizontal route in conventional transistors. IBM expects that within two years the transistors will drive chips used in communications equipment to 100 GHz—five times faster than today's chips. (The transistors, though, are incompatible with computer processors.) The little super-silicon transistors still have a way to go before they can switch quickly enough to keep up with the theoretical limit of fiber-optic communications. In the June 28 *Nature*, researchers at Lucent Technologies calculated the limit to be approximately 100 terabits per strand of fiber. Current data transmission rates run as high as 1.6 terabits per second over a single strand.

—Mariama Orange



PSYCHOLOGY

You Forgot to Remember

Recent studies illustrate how easy it is to create false memories. Jacquie Pickrell and Elizabeth Loftus of the University of Washington reported at a recent American Psychological Society conference in Toronto that many visitors to Disneyland concluded that they had met Bugs Bunny, a Warner Bros. character ordinarily not seen at the happiest place on Earth. The psychologists had subjects read fake Disney ads, some of which mentioned Bugs—and sometimes in the presence of a cardboard cutout of him. About one third of those later exposed to Bugs believed that they had encountered and even shook hands with the rascally rabbit at Disneyland. Other researchers found that people can fabricate false images because of “causal inference.” Viewing the result of an action (oranges on the ground, say), people will recall spotting the cause (someone reaching for an orange at the bottom to upset the stack) even if they never saw such an image. The study, which helps to explain errors in eyewitness accounts, is available at www.apa.org/journals/xlm/press_releases/july_2001/xlm274931.html

—Philip Yam

MEDICINE

Peace in the Nonobese

A simple treatment might one day relieve type 1 diabetics of daily finger pricking and insulin injections. In type 1 diabetes, immune cells wage war on insulin-secreting islet cells in the pancreas, resulting in improper blood glucose levels. (Type 2 diabetes results from cells' becoming insensitive to insulin, often as a result of obesity.) Working with what they call non-obese diabetic mice, researchers at Massachusetts General Hospital retrained the attacking immune system to ignore any surviving islet cells. The investigators first killed off the attack cells, which are abnormal, and then injected normal immune cells from healthy donor mice. As a result, diabetic mice began producing islet-friendly immune cells. The approach seemed to effect a permanent reversal: the glucose levels of some 75 percent of the mice returned to normal. The study appears in the July 1 *Journal of Clinical Investigation*.

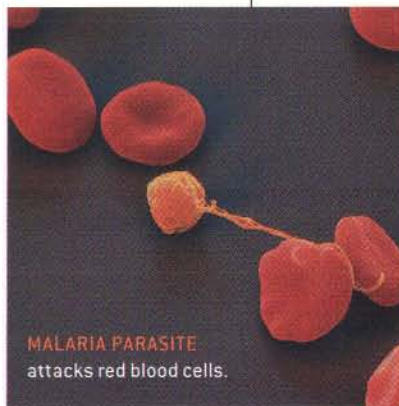
—Mariama Orange

EVOLUTION

Infectious Selection

Infectious disease can be a powerful driving force in evolution. Recently scientists led by Sarah Tishkoff of the University of Maryland found that changes in the frequency of certain forms, or alleles, of the gene for glucose-6-phosphate dehydrogenase (G6PD) within human populations roughly mirror the history of malaria. Some mutations of the gene result in reduced activity of G6PD, producing anemia and, more advantageously, moderate resistance to malaria. Looking at the history of the various forms of the G6PD gene within populations most affected by malaria, such as those in Africa and India, the researchers discovered that the alleles that encode for G6PD deficiency arose during the same approximate time that malaria became more deadly. Moreover, the alleles spread more rapidly within hard-hit populations than chance alone would suggest. These results, in the July 20 *Science*, indicate that selective pressure from malaria can maintain and promote otherwise deleterious alleles in the human gene pool.

—Alison McCook



MALARIA PARASITE attacks red blood cells.

GEOCHEMISTRY

More Than Shade

When trees first took over the continents about 380 million years ago, they changed the world in an unexpected way. Researchers knew that trees absorbed much more carbon dioxide from the atmosphere than their moss and alga predecessors. But according to computer models of the long-term carbon cycle by Yale University geochemist Robert A. Berner and his colleagues, as photosynthesis hit an unprecedented high, the atmosphere also became twice as rich in oxygen as it is today—40 percent relative to 21 percent. That means trees could have been responsible for the evolution of gigantic insects, such as the dragonflies with 70-centimeter wingspans known to exist at the time. An insect's size depends in part on how much atmospheric oxygen is available to diffuse passively into its body. Berner presented the findings in June at the Earth System Processes conference in Edinburgh, Scotland.

—Sarah Simpson



TREES may have been harbingers of big bugs.

WWW.SCIAM.COM/NEWS BRIEF BITS

- In Ethiopia, researchers uncovered the fossils of what appears to be **humanity's oldest ancestor**, who is thought to have lived between 5.2 million and 5.8 million years ago. /071201/3.html
- Scientists have created patterned glass surfaces on which living **nerve cells can wire themselves to electrodes**; the research may lead to better implants, prosthetics and biosensors. /071001/1.html
- The friction-free superfluid helium 3 can act as a **quantum gyroscope**, producing a whistling sound that gets louder or quieter depending on the orientation of the earth's axis of rotation. /070901/3.html
- A study has found that **clones are not genetically identical** to the donor animals; in fact, the clones sometimes exhibit dangerously different patterns of gene expression. /070601/1.html

Measuring Bad Behavior

FBI CRIME STATISTICS: USE WITH CAUTION BY RODGER DOYLE

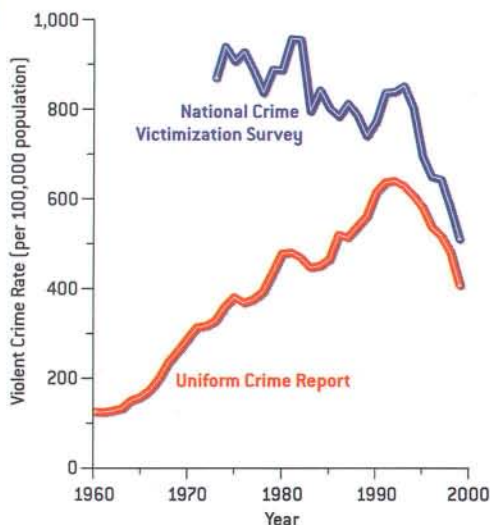
THE FBI'S INDEX CRIMES

- Criminal homicide—excludes attempted homicide
- Rape of women by force or threat of force—excludes statutory rape
- Robbery: taking by force or threat of force anything of value—includes attempted robbery
- Aggravated assault: attack with intent of inflicting severe bodily injury, usually with a weapon—excludes simple assault (assault without a weapon resulting in little or no injury)
- Burglary: unlawful entry or attempted entry to commit a felony or theft
- Larceny, theft: unlawful taking or attempted taking of property—excludes motor vehicles
- Motor vehicle theft—includes attempted theft
- Arson—includes attempted arson

The Bureau of Justice Statistics's National Crime Victimization Surveys provide data on the same crimes except for homicide, arson, crimes committed against commercial establishments and crimes against children younger than 12.

The Uniform Crime Reports (UCR), produced by the Federal Bureau of Investigation, have figured prominently in discussions of crime since at least the Nixon era, but their reliability has long been suspect. A major reason is substantial underreporting. For a variety of reasons, including distrust of law-enforcement officials, many crimes are not reported to local police departments, the source of the FBI data. Furthermore, the number of crimes that police departments report can vary from year to year depending on budgets. The FBI cannot legally enforce the cooperation of local police departments and state agencies, and so it is not surprising that for several years in the 1990s, six states (the largest in terms of population was Illinois) supplied no data, forcing the FBI to estimate the number of crimes in those states.

Local police sometimes cook the books, either underreporting to make crime in their area appear to be under control or overreporting to support requests for more funding. Fabrication of this kind has presumably declined as police departments have become more publicly accountable in the past few decades, but it still persists, as recent reports of data manipulation in New York City, Philadelphia and Boca Raton, Fla., testify.



SOURCES: FBI and Bureau of Justice Statistics. Violent crime statistics shown above include robbery (except of businesses), rape and aggravated assault and exclude crimes against children younger than 12. Victimization data exclude incidents not reported to the police.

To supplement the UCR, the Bureau of Justice Statistics in 1973 started an annual survey of about 50,000 households designed to count the number of crime victims. Many respondents did not correctly recall when a crime was committed, putting it in the wrong year, for example, and some even failed to recall crimes in which they were known to be victims. Despite such limitations, however, the National Crime Victimization Surveys, as they are called, are a reasonably good guide to overall crime trends, as shown by their rough concordance with data on homicide, the best recorded of the UCR categories.

The chart compares the UCR and victimization data in terms of serious violent crime. The UCR numbers are not only much lower because of incomplete reporting but are misleading as an indicator of violent crime trends because reporting improved over the past several decades. The extent of the improvement is suggested by the growing convergence of the UCR with the victimization survey: In 1973 the number of violent crimes reported by the UCR totaled only 38 percent of those reported by the survey but increased gradually to between 80 and 84 percent in the second half of the 1990s and is expected to rise further. Improved reporting, together with a newly introduced system that provides greater detail on crime incidents, has increased the usefulness of the UCR as an analytic tool, but as an indicator of national crime trends it still remains deficient.

The UCR covers eight types of violent and property offenses—so-called index crimes—but excludes others, such as drug violations, simple assault, vandalism, prostitution, statutory rape, child abuse, and white-collar offenses such as embezzlement, stock fraud, forgery, counterfeiting and cybercrime. These types of infractions are excluded from the index because they are not readily brought to the attention of the police (for example, embezzlement), are rare (kidnapping) or are not serious enough to warrant inclusion (disorderly conduct).

Rodger Doyle can be reached at rdoyl2@adelphia.net



Nano Nonsense and Cryonics

True believers seek redemption from the sin of death By MICHAEL SHERMER

Cryonicists believe that people can be frozen immediately after death and reanimated later when the cure for what ailed them is found. To see the flaw in this system, thaw out a can of frozen strawberries. During freezing, the water within each cell expands, crystallizes, and ruptures the cell membranes. When defrosted, all the intracellular goo oozes out, turning your strawberries into runny mush. This is your brain on cryonics.

Cryonicists recognize this detriment and turn to nanotechnology for a solution. Microscopic machines will be injected into the defrosting "patient" to repair the body molecule by molecule until the trillions of cells are restored and the person can be resuscitated. Every religion needs its gods, and this scientific vision has a trinity in Robert C. W. Ettinger (*The Prospect of Immortality*), K. Eric Drexler (*Engines of Creation*) and Ralph C. Merkle (*The Molecular Repair of the Brain*), who preach that nanocryonics will wash away the sin of death. These works are built on the premise that if you are cremated or buried, you have zero probability of being resurrected—cryonics is better than everlasting nothingness.

Is it? That depends on how much time, effort and money (\$120,000 for a full-body freeze or \$50,000 for just the head) you are willing to invest for odds of success only slightly higher than zero. It takes a blindly optimistic faith in the illimitable power of science to solve any and all problems, including death. Look how far we've come in just a century, believers argue—from the Wright brothers to Neil Armstrong in only 66 years. Extrapolate these trends out 1,000 years, or 10,000, and immortality is virtually certain.

I want to believe the cryonicists. Really I do. I gave up on religion in college, but I often slip back into my former evangelical fervor, now directed toward the wonders of science and nature. But this is precisely why I'm skeptical. It is too much like religion: it promises everything, delivers nothing (but hope) and is based almost entirely on faith in the future. And if Ettinger,

Drexler and Merkle are the trinity of this scientific sect, then F. M. Esfandiary is its Saul. Esfandiary, on the road to his personal Damascus, changed his name to FM-2030 (the number signifying his 100th birthday and the year nanotechnology is predicted to make cryonics successful) and declared, "I have no age. Am born and reborn every day. I intend to live forever. Barring an accident I probably will."

Esfandiary forgot about cancer, a pancreatic form of which killed him on July 8, 2000. FM-2030—or more precisely, his head—now resides in a vat of liquid nitrogen at the Alcor Life Extension Foundation in Scottsdale, Ariz., but his legacy lives on among his fellow "transhumanists" (they have moved beyond human) and "extropians" (they are against entropy).

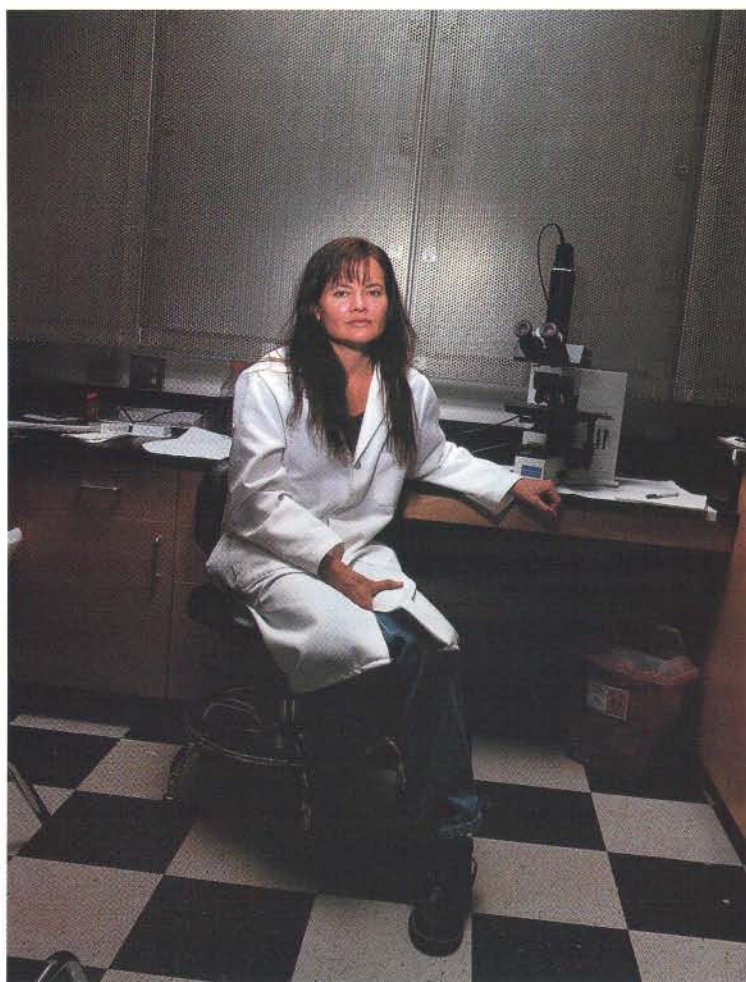
This is what I call "borderlands science," because it dwells in that fuzzy region of claims that have yet to pass any tests but have some basis, however remote, in reality. It is not impossible for cryonics to succeed; it is just exceptionally unlikely. The rub in exploring the borderlands is finding that balance between being open-minded enough to accept radical new ideas but not so open-minded that your brains fall out. My credulity module is glad that some scientists are devoting themselves to the problem of mortality. My skepticism module, however, recognizes that transhumanistic-extropian cryonics is uncomfortably close to religion. I worry, as Matthew Arnold did in his 1852 poem "Hymn of Empedocles," that we will "feign a bliss/ Of doubtful future date,/ And while we dream on this/ Lose all our present state,/ And relegate to worlds yet distant our repose."

Michael Shermer is publisher of Skeptic magazine (www.skeptic.com) and author of *How We Believe* and *The Borderlands of Science*.

The rub is finding that balance between being open-minded enough to accept radical new ideas but not so open-minded that your brains fall out.

Young Cells in Old Brains

The paradigm-shifting conclusion that adult brains can grow new neurons owes a lot to Elizabeth Gould's rats and monkeys By MARGUERITE HOLLOWAY



ELIZABETH GOULD: CHANGING MINDS

- **Past thinking:** Memories are stored by locked-in neural connections.
Present: The brain can add neurons, perhaps to establish new memories.
- **Hope for dementia:** New neurons seem able to migrate, suggesting that therapeutic cells can be guided to areas damaged by disease or injury.
- **Use it or lose it:** In lab animals not kept in a stimulating cognitive environment, "most new neurons will die within a few weeks."

PRINCETON, N.J.—Reunion weekend at Princeton University, and the shady Gothic campus has been inundated by spring showers and men in boaters and natty orange seersucker jackets. Tents and small groups of murmuring alumni dot the courtyards. Everything proper, seemingly in its place. In Green Hall, however, the same order does not prevail. Elizabeth Gould's laboratory is undergoing construction, and the neuroscientist herself would not be mistaken for an alum: her plaid blue workman's shirt hangs loosely and unbuttoned over a T-shirt and jeans, and she confesses she often feels out of place on the conservative campus.

Against a backdrop of tidy ideas about the brain, Gould and her colleagues have been messing things up and, in the process, contributing to some of the most exciting findings of the past decade. Her work—and that of several other neuroscientists—has made clear that new neurons are produced in certain areas of the adult brains of mammals, including primates. Moreover, these cells can be killed off by stress and unchallenging environments but thrive in enriched settings where animals are learning, and they may play a role in memory.

Until recently, dogma held that mature brains were static: no cells were born, except in the olfactory bulb. One of the cornerstones of this understanding came from studies by Pasko Rakic of Yale University, who examined macaque monkeys and found no evidence of the creation of nerve cells, a process called neurogenesis. The prevailing view has since held that primates—and, indeed, mammals in general—are born with all the neurons they are going to have. Such neural stability was considered necessary for long-term memory. So in the late 1980s when Gould, who was then researching the effect of hormones on the brain as a postdoctoral fellow in the laboratory of Bruce S. McEwen at the Rockefeller University, saw evidence of new neurons in the rat hippocampus, she was perplexed. Gould knew from the pioneering work of Fernando Nottebohm, also at Rockefeller, that neurogenesis occurred in adult birds—ca-

naries and zebra finches, for instance, grow nerve cells to learn new songs—but she and her lab mates knew of no mammalian parallel. “We were really puzzled,” she recalls. “It wasn’t until we delved far enough back into the literature that we found evidence that new neurons are produced in the hippocampus.”

Those earlier studies had never been widely noticed. Beginning in the 1960s Joseph Altman, now professor emeritus at Purdue University, and neurologist Michael S. Kaplan independently recorded neurogenesis in rats and other mammals. They saw growth in the olfactory bulb, in the hippocampus—a region important to memory—and, most strikingly, in the neocortex, which is the part of the brain involved in higher thinking. “But nobody picked up on the results,” Gould says. “It is a classic example of something appearing before its time.”

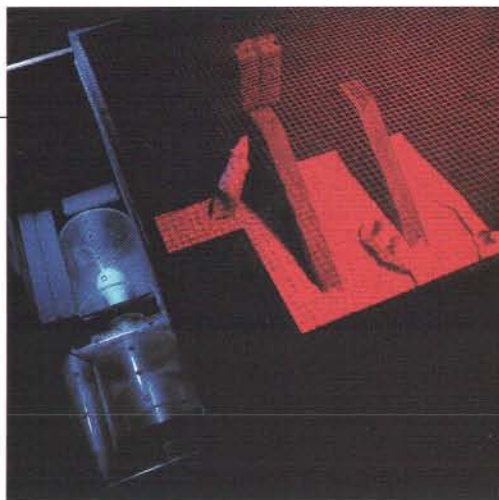
In her work with rats, Gould verified that when she altered the normal hormonal bath the hippocampus received, cells died and, apparently to compensate, more cells were born. “That was really the beginning of my interest in neurogenesis and my realization that it happened,” she says. Her first papers on the phenomenon, published in 1992 and 1993, did not attract much attention.

Gould went on to do experiments clarifying aspects of neurogenesis. She found that stress suppressed the creation of neurons and that lesions in the hippocampus triggered the development of new cells—something she considers significant because it implies that the brain can heal, or be induced to heal, after injury.

In 1997 Gould moved to Princeton as an assistant professor. Over the next few years she and her co-workers reported that new neurons survived if animals lived in complex environments and learned tasks, findings also documented in mice by Fred H. Gage of the Salk Institute for Biological Studies in La Jolla, Calif.

Gould’s work in rats contradicting the status quo had already put her out on a limb. Then she observed that new neurons are found in the hippocampus of marmoset monkeys and macaques. News of neurogenesis in primates was met with skepticism and stiff opposition, and some suggested her methods were flawed. She was soon vindicated, however, thanks to confirmatory work by Rakic in macaques and by Gage in the human hippocampus. The findings catalyzed widespread interest because they introduced the possibility of repairing the brain and elucidating memory formation.

For Gould, the sudden splash of attention has been disorienting—and she does not relish it, particularly when it takes her away from her experiments. She says she is happiest in the lab, working under the microscope with brain slices, which she finds beautiful and which recall a childhood interest in being an artist.



VISIBLE RAT BURROWS enable Gould to observe behavior and experiences that might lead to new neurons.

And she has liked being in a quiet field of research, one she chose when studying psychology at the University of California at Los Angeles. “I have no interest in doing experiments that someone else is going to do a month later if I don’t get around to it,” she says. “You have to pick things to do that are really intriguing to you, things that you are really curious about—not just because you want to publish on them before anyone else does.”

Her curiosity is taking her in several directions these days. An out-

standing question centers on what role new hippocampal neurons play. Do they establish new circuits or memories? Or do they replace old neurons in established circuits? This year Gould and her colleagues reported that the neurons are involved in the creation of trace memories—memories important to temporal information. “We had evidence that the new cells were affected by learning, and this is evidence that the new cells are necessary for learning,” Gould explains. She now intends to do similar studies in marmosets, to see whether her discoveries about rats will prove true for primates.

The 39-year-old Gould is also repeating and extending work of a few years ago in which she found neurogenesis in the neocortex of macaques, a finding that remains controversial and that would be highly significant because of the importance of the cortex. Although no one has published a replication so far, William T. Greenough of the University of Illinois says Gould’s findings “do not surprise me. We have unpublished data in rats that support the same thing.”

In addition, Gould has begun investigating the role of sleep deprivation in neurogenesis, an interest triggered by the birth of her third child last year. “I never really thought about the sleep aspect until I wasn’t getting any,” she says, laughing. And she is intrigued by the possibility that much of what we have come to understand from laboratory settings may be skewed.

“Our laboratory animals are very abnormal,” Gould notes. “They have unlimited access to food and water, and they have no interesting cognitive experiences at all. We know that if you house an animal in that setting, most of its new neurons will die within a few weeks after they are produced.” Gould is designing environments that are closer to the ones rats and marmosets experience in the wild, hoping to get closer to the truth about the brain. “It really raises the issue of whether a lot of the things we are looking at are really deprivation effects.”

Potentially shifting another paradigm doesn’t faze Gould. “There has to be some fresh perspective, something new that you can bring to the work that other people wouldn’t see,” she says. “Otherwise you are not making a real contribution, and you might as well just step aside and find something else to do.” ■

Little Big Science

Nanotechnology is all the rage. But will it meet its ambitious goals? And what the heck is it?

By Gary Stix

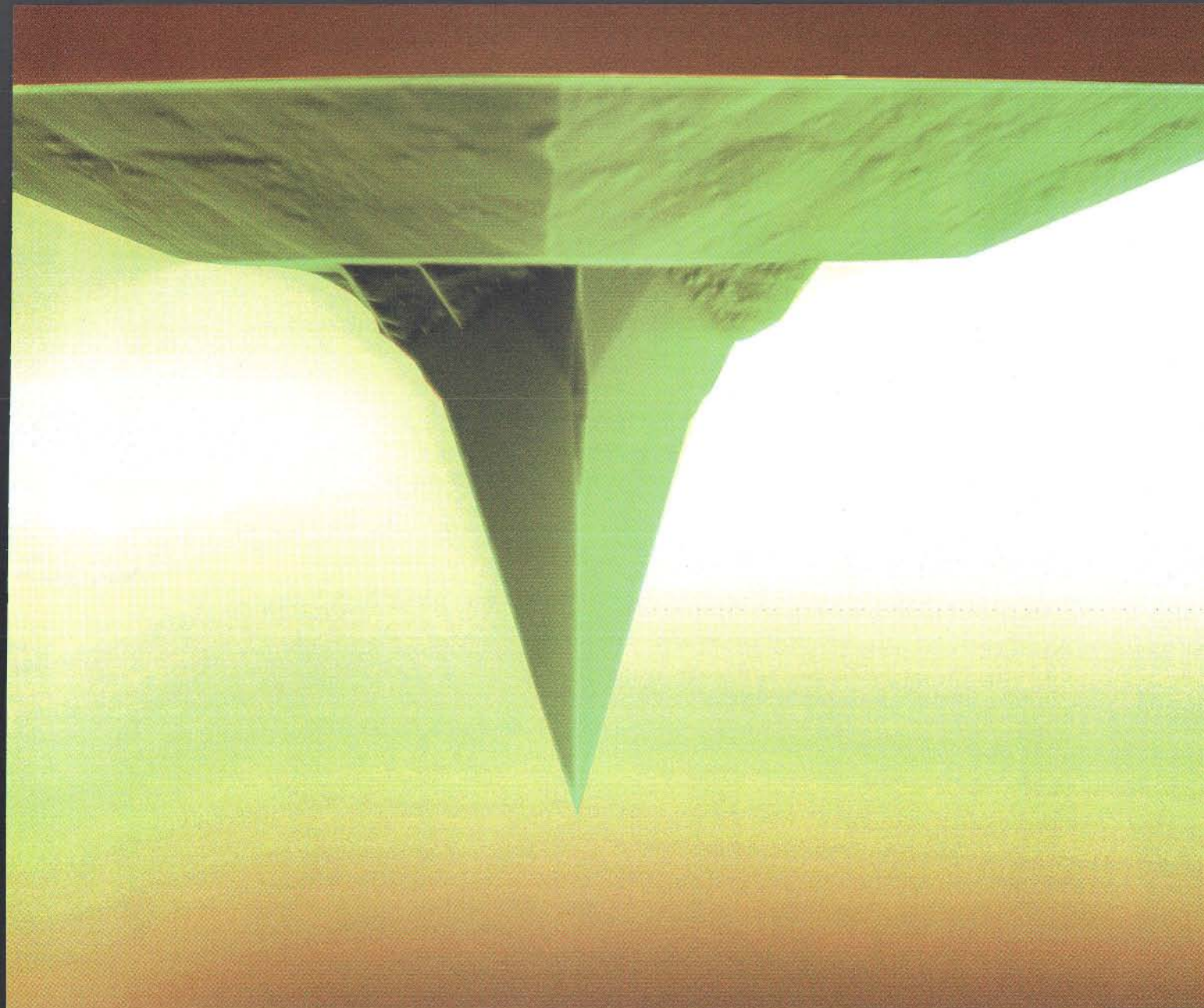
Albert Einstein, as part of his doctoral dissertation, calculated the size of a single sugar molecule from experimental data on the diffusion of sugar in water. His work showed that each molecule measures about a nanometer in diameter. At a billionth of a meter, a nanometer is the essence of small. The width of 10 hydrogen atoms laid side by side, it is one thousandth the length of a typical bacterium, one millionth the size of a pinhead, one billionth the length of Michael Jordan's well-muscled legs. One nanometer is also precisely the dimension of a big windfall for research.

Almost 100 years after Einstein's insight, the nanometer scale looms large on the research agenda. If Einstein were a graduate student today probing for a career path, a doctoral adviser would enjoin him to think small: "Nanotech, Albert, nanotech" would be the message conveyed.

After biomedical research and defense—fighting cancer and building missile shields still take precedence—nanotechnology has become the most highly energized discipline in science and

technology. The field is a vast grab bag of stuff that has to do with creating tiny things that sometimes just happen to be useful. It borrows liberally from condensed-matter physics, engineering, molecular biology and large swaths of chemistry. Researchers who once called themselves materials scientists or organic chemists have transmuted into nanotechnologists.

Purist academic types might prefer to describe themselves as mesoscale engineers. But it's "nano" that generates the buzz. Probably not since Du Pont coined its corporate slogan "better things for better living through chemistry" have scientists who engage in molecular manipulation so adeptly captured and held public attention—in this case, the votes of lawmakers in Washington who hold the research purse strings. "You need to come up with new, exciting, cutting-edge, at-the-frontier things in order to convince the budget- and policy-making apparatus to give you more money," remarks Duncan Moore, a former White House official who helped to organize the Clinton administration's funding push for nanotechnology.



With recognition has come lots of money—lots, that is, for something that isn't a missile shield. The National Nanotechnology Initiative (NNI), announced early last year by President Bill Clinton, is a multiagency program intended to provide a big funding boost to nanoscience and engineering. The \$422-million budget in the federal fiscal year that ends September 30 marks a 56 percent jump in nano spending from a year earlier. The initiative is on track to be augmented for fiscal year 2002 by another 23 percent even while the Bush administration has proposed cuts to the funding programs of most of the federal agencies that support research and development (see the NNI Web site at www.nano.gov). Nano mania flourishes everywhere. More than 30 nanotechnology research centers and interdisciplinary groups have sprouted at universities; fewer than 10 existed two years ago. Nanoism does not, moreover, confine itself to the U.S. In other countries, total funding for nanotechnology jumped from \$316 million in 1997 to about \$835 million this year, according to the National Science Foundation (NSF).

TIP OF ATOMIC FORCE MICROSCOPE used to probe surfaces and manipulate molecules symbolizes the nanotechnology revolution.

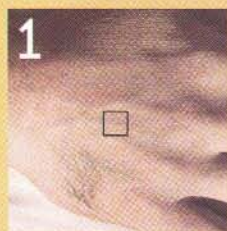
Interest in nano is also fueled, in an aberrant way, by the visions of a fringe element of futurists who muse on biblical life spans, on unlimited wealth and, conversely, on a holocaust brought about by legions of uncontrollable self-replicating robots only slightly bigger than Einstein's sugar molecules. (Check out the Web site for *NanoTechnology* magazine—<http://planet-hawaii.com/nanozine/>—if you want to learn about an “era of self-replicating consumer goods, super-health, super-economy and inventions impossible to fabricate with first wave industrialization.”)

When Clinton introduced the nanotechnology initiative in a speech last year, he was long on vision and short on specifics: nanotech, he noted, might one day store the Library of Congress on a device the size of a sugar cube or produce materials with 10 times the strength of steel at a mere fraction of its

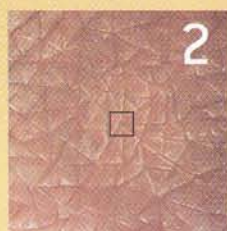
Macro, Micro, Nano

How small is a nanometer? Stepping down in size by powers of 10 takes you from the back of a hand to, at one nanometer, a view of atoms in the building blocks of DNA. The edge of each image denotes a length 10 times longer than its next smallest neighbor. The black square frames the size of the next scene inward.

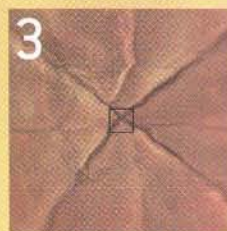
HAND



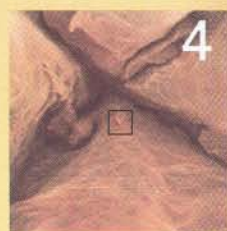
10 centimeters



1 centimeter



1 millimeter



100 microns

WHITE BLOOD CELL



10 microns



1 micron

DNA



100 nanometers



10 nanometers



1 nanometer

From the classic book *Powers of Ten*, by Philip and Phyllis Morrison and the office of Charles and Ray Eames.

weight. But this wasn't just the meanderings of a starry-eyed politician. Surprisingly, the science establishment itself is a little unclear about what it really means when it invokes nano. "It depends on whom you ask," Stanford biophysicist Steven M. Block told a National Institutes of Health symposium on nanotechnology last year in a talk that tried to define the subject. "Some folks apparently reserve the word to mean whatever it is they do as opposed to whatever it is anyone else does."

What's in a Name?

THE DEFINITION is indeed slippery. Some of nanotechnology isn't nano, dealing instead with structures on the micron scale (millionths of a meter), 1,000 times or more larger than a nanometer. Also, nanotechnology, in many cases, isn't technology. Rather it involves basic research on structures having at least one dimension of about one to several hundred nanometers. (In that sense, Einstein was more a nanoscientist than a technologist.) To add still more confusion, some nanotechnology has been around for a while: nano-size carbon black particles (a.k.a. high-tech soot) have gone into tires for 100 years as a reinforcing additive, long before the prefix "nano" ever created a stir. For that matter, a vaccine, which often consists of one or more proteins with nanoscale dimensions, might also qualify.

But there is a *there* there in both nanoscience and nanotechnology. The nanoworld is a weird borderland between the realm of individual atoms and molecules (where quantum mechanics rules) and the macroworld (where the bulk properties of materials emerge from the collective behavior of trillions of atoms, whether that material is a steel beam or the cream filling in an OreO). At the bottom end, in the region of one nanometer, nanoland bumps up against the basic building blocks of matter. As such, it defines the smallest natural structures and sets a hard limit to shrinkage: you just can't build things any smaller.

Nature has created nanostructures for millennia. But Mihail C. Roco, the NSF official who oversees the nanotechnology initiative, offers a more restrictive definition. The emerging field—new versus old nanotech—deals with materials and systems having these key properties: they have at least one dimension of about one to 100 nanometers, they are designed through processes that exhibit fundamental control over the physical and chemical attributes of molecular-scale structures, and they can be combined to form larger structures. The intense interest in using nanostructures stems from the idea that they may boast superior electrical, chemical, mechanical or optical properties—at least in theory. (See "Plenty of Room, Indeed," by Michael Roukes, on page 42, for a discussion of why smaller is not always better.)

Real-world nano, fitting Roco's definition, does exist. Sandwiching several nonmagnetic layers, one of which is less than a nanometer thick, between magnetic layers can produce sensors for disk drives with many times the sensitivity of previous devices, allowing more bits to be packed on the surface of each disk. Since they were first introduced in 1997, these gi-

Once conventional silicon electronics goes bust, new nanoelectronic devices are a good bet to replace them. A likely wager, though not a sure one.

ant magnetoresistive heads have served as an enabling technology for the multibillion-dollar storage industry.

New tools capable of imaging and manipulating single molecules or atoms have ushered in the new age of nano. The icons of this revolution are scanning probe microscopes—the scanning tunneling microscope and the atomic force microscope, among others—capable of creating pictures of individual atoms or moving them from place to place. The IBM Zurich Research Laboratory has even mounted the sharp, nanometer-scale tips used in atomic force microscopes onto more than 1,000 microscopic cantilevers on a microchip. The tips in the Millipede device can write digital bits on a polymer sheet. The technique could lead to a data storage device that achieves 20 times or more the density of today's best disk drives.

Varied approaches to fabricating nanostructures have emerged in the nanoworld. Like sculptors, so-called top-down practitioners chisel out or add bulk material to a surface. Microchips, which now boast circuit lines of little more than 100 nanometers, are about to become the most notable example. In contrast, bottom-up manufacturers use self-assembly processes to put together larger structures—atoms or molecules that make ordered arrangements spontaneously, given the right conditions. Nanotubes—graphite cylinders with unusual electrical properties—are a good example of self-assembled nanostructures [see “The Art of Building Small,” by George M. Whitesides and J. Christopher Love, on page 32].

Beyond Silicon

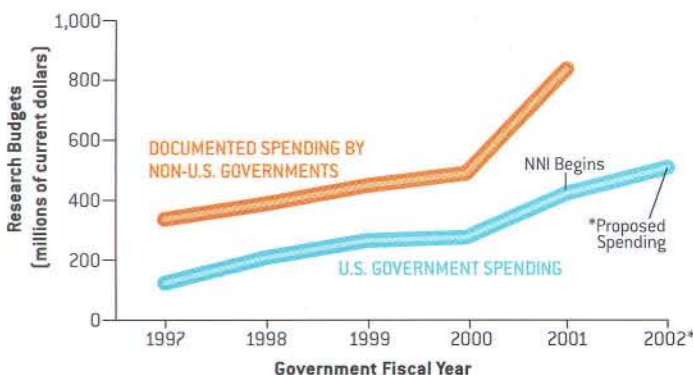
THE DWINDLING SIZE of circuits in electronic chips drives much of the interest in nano. Computer companies with large research laboratories, such as IBM and Hewlett-Packard, have substantial nano programs. Once conventional silicon electronics goes bust—probably sometime in the next 10 to 25 years—it's a good bet that new nanotechnological electronic devices will replace them. A likely wager, though not a sure one. No one knows whether manufacturing electronics using nanotubes or some other novel material will allow the relentless improvements in chip performance without a corresponding increase in cost that characterizes silicon chipmaking [see “The Incredible Shrinking Circuit,” by Charles M. Lieber, on page 50].

Even if molecular-scale transistors don't crunch zeroes and ones in the Pentium XXV, the electronics fashioned by nanotechnologists may make their way into devices that reveal the secrets of the ultimate small machine: the biological cell. Bio-nano, in fact, is finding real applications before the advent of postsilicon nanocomputers [see “Less Is More in Medicine,” by A. Paul Alivisatos, on page 58]. Relatively few nanotags made of a semiconductor material are needed to detect cellular activity, as opposed to the billions or trillions of transis-

tors that must all work together to function in a nanocomputer. One company, Quantum Dot Corporation, has already emerged to exploit semiconductor quantum dots as labels in biological experiments, drug-discovery research, and diagnostic tests, among other applications.

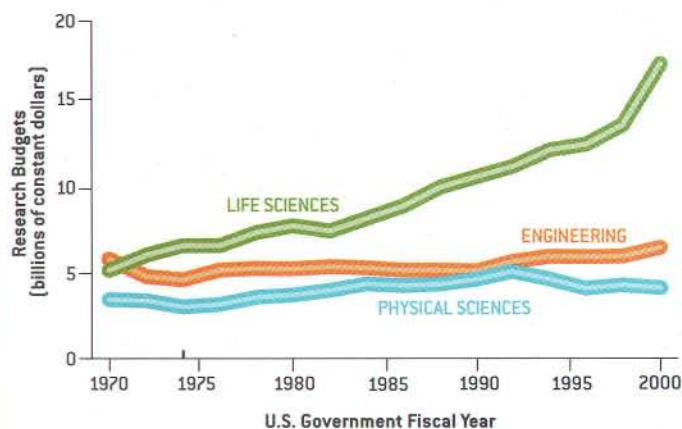
Outside biology, the earliest wave of products involves using nanoparticles for improving basic material properties. For instance, Nanophase Technologies, one of the few companies in this field that are publicly traded, produces nano-size zinc oxide particles for use in sunscreen, making the usually white-colored cream transparent because the tiny particles don't scatter visible light.

FUNDING FOR NANOTECHNOLOGY



SOURCES: U.S. Senate briefing on nanotechnology, May 24, 2001, and National Science Foundation

TRENDS IN FEDERAL RESEARCH FOR SELECTED DISCIPLINES



SOURCE: National Science Foundation

UPTICK: The National Nanotechnology Initiative (NNI), begun in fiscal year 2001, helps to keep the U.S. competitive with world spending [top]. It also provides a monetary injection for the physical sciences and engineering, where funding has been flat by comparison with the life sciences [bottom].

Nanotechnology's bid for respectability is colored by the word's association with a cabal of futurists who foresee nano as a pathway to utopia.

A Few 10^{-9} Milestones

3.5 billion years ago The first living cells emerge. Cells house nanoscale biomachines that perform such tasks as manipulating genetic material and supplying energy.

400 B.C. Democritus coins the word "atom," which means "not cleavable" in ancient Greek.

1905 Albert Einstein publishes a paper that estimates the diameter of a sugar molecule as about one nanometer.

1931 Max Knoll and Ernst Ruska develop the electron microscope, which enables subnanometer imaging.

1959 Richard Feynman gives his famed talk "There's Plenty of Room at the Bottom," on the prospects for miniaturization.

1968 Alfred Y. Cho and John Arthur of Bell Laboratories and their colleagues invent molecular-beam epitaxy, a technique that can deposit single atomic layers on a surface.

1974 Norio Taniguchi conceives the word "nanotechnology" to signify machining with tolerances of less than a micron.

1981 Gerd Binnig and Heinrich Rohrer create the scanning tunneling microscope, which can image individual atoms.

1985 Robert F. Curl, Jr., Harold W. Kroto and Richard E. Smalley discover buckminsterfullerenes, also known as buckyballs, which measure about a nanometer in diameter.

1986 K. Eric Drexler publishes *Engines of Creation*, a futuristic book that popularizes nanotechnology.

1989 Donald M. Eigler of IBM writes the letters of his company's name using individual xenon atoms.

1991 Sumio Iijima of NEC in Tsukuba, Japan, discovers carbon nanotubes.

1993 Warren Robinett of the University of North Carolina and R. Stanley Williams of the University of California at Los Angeles devise a virtual-reality system connected to a scanning tunneling microscope that lets the user see and touch atoms.

1998 Cees Dekker's group at the Delft University of Technology in the Netherlands creates a transistor from a carbon nanotube.

1999 James M. Tour, now at Rice University, and Mark A. Reed of Yale University demonstrate that single molecules can act as molecular switches.

2000 The Clinton administration announces the National Nanotechnology Initiative, which provides a big boost in funding and gives the field greater visibility.

2000 Eigler and other researchers devise a quantum mirage. Placing a magnetic atom at one focus of an elliptical ring of atoms creates a mirage of the same atom at another focus, a possible means of transmitting information without wires.

The government's nanotech initiative goes beyond sunscreen. It envisages that nanostructured materials may help reduce the size, weight and power requirements of spacecraft, create green manufacturing processes that minimize the generation of unwanted by-products, and form the basis of molecularly engineered biodegradable pesticides. The field has such a broad scope—and basic research is still so new in some nanosubspecialties—that worries have arisen about its ability to deliver on ambitious technology goals that may take 20 years to achieve. "While nanotechnology may hold great promise, some scientists contend that the field's definition is too vague and that much of its 'hype' may not match the reality of present scientific speculation," noted a Congressional Research Service report last year.

Nanodreams

ANY ADVANCED RESEARCH carries inherent risks. But nanotechnology bears a special burden. The field's bid for respectability is colored by the association of the word with a cabal of futurists who foresee nano as a pathway to a technoutopia: unparalleled prosperity, pollution-free industry, even something resembling eternal life.

In 1986—five years after IBM researchers Gerd Binnig and Heinrich Rohrer invented the scanning tunneling microscope, which garnered them the Nobel Prize—the book *Engines of Creation*, by K. Eric Drexler, created a sensation for its depiction of godlike control over matter. The book describes self-replicating nanomachines that could produce virtually any material good, while reversing global warming, curing disease and dramatically extending life spans. Scientists with tenured faculty positions and NSF grants ridiculed these visions, noting that their fundamental improbability made them an absurd projection of what the future holds.

But the visionary scent that has surrounded nanotechnology ever since may provide some unforeseen benefits. To many nonscientists, Drexler's projections for nanotechnology straddled the border between science and fiction in a compelling way. Talk of cell-repair machines that would eliminate aging as we know it and of home food-growing machines that could produce victuals without killing anything helped to create a fascination with the small that genuine scientists, consciously or not, would later use to draw attention to their work on more mundane but eminently more real projects. Certainly labeling a research proposal "nanotechnology" has a more alluring ring than calling it "applied mesoscale materials science."

Less directly, Drexler's work may actually draw people into science. His imaginings have inspired a rich vein of science-fiction literature [see "Shamans of Small," by Graham P.

Collins, on page 78]. As a subgenre of science fiction—rather than a literal prediction of the future—books about Drexlerian nanotechnology may serve the same function as *Star Trek* does in stimulating a teenager's interest in space, a passion that sometimes leads to a career in aeronautics or astrophysics.

The danger comes when intelligent people take Drexler's predictions at face value. Drexlerian nanotechnology drew renewed publicity last year when a morose Bill Joy, the chief scientist of Sun Microsystems, worried in the magazine *Wired* about the implications of nanorobots that could multiply uncontrollably. A spreading mass of self-replicating robots—what Drexler has labeled “gray goo”—could pose enough of a threat to society, he mused, that we should consider stopping development of nanotechnology. But that suggestion diverts attention from the real nano goo: chemical and biological weapons.

Among real chemists and materials scientists who have now become nanotechnologists, Drexler's predictions have assumed a certain quaintness; science is nowhere near to being able to produce nanoscopic machines that can help revive frozen brains from suspended animation. (Essays by Drexler and his critics, including Nobel Prize winner Richard E. Smalley, appear in this issue.) Zyvex, a company started by a software magnate enticed by Drexlerian nanotechnology, has recognized how difficult it will be to create robots at the nanometer scale; the company is now dabbling with much larger micromechanical elements, which Drexler has disparaged in his books [see “Nanobot Construction Crews,” by Steven Ashley, on page 76].

Even beyond meditations on gray goo, the nanotech field struggles for cohesion. Some of the research would have proceeded regardless of its label. Fusing “nano” and “technology” was an after-the-fact designation: IBM would have forged ahead in building giant magnetoresistive heads whether or not the research it was doing was labeled nanotechnology.

For the field to establish itself as a grand unifier of the applied sciences, it must demonstrate the usefulness of grouping widely disparate endeavors. Can scientists and engineers doing research on nanopowders for sunscreens share a common set of interests with those working on DNA computing? In some cases, these crossover dreams may be justified. A semiconductor quantum dot originally developed for electronics and now being deployed to detect biological activity in cells is a compelling proof of principle for these types of transdisciplinary endeavors.

If the nano concept holds together, it could, in fact, lay the groundwork for a new industrial revolution. But to succeed, it will need to discard not only fluff about nanorobots that bring cadavers back from a deep freeze but also the overheated rhetoric that can derail any big new funding effort. Most important, the basic nanoscience must be forthcoming to identify worthwhile nanotechnologies to pursue. Distinguishing between what's real and what's not in nano throughout this period of extended exploration will remain no small task. ■

Gary Stix is Scientific American's special projects editor.

Nano for Sale

Not all nanotechnology lies 20 years hence, as the following sampling of already commercialized applications indicates.

APPLICATION: CATALYSTS

COMPANY: EXXONMOBIL

DESCRIPTION: Zeolites, minerals with pore sizes of less than one nanometer, serve as more efficient catalysts to break down, or crack, large hydrocarbon molecules to form gasoline.

APPLICATION: DATA STORAGE

COMPANY: IBM

DESCRIPTION: In the past few years, disk drives have added nanoscale layering—which exploits the giant magnetoresistive effect—to attain highly dense data storage.

APPLICATION: DRUG DELIVERY

COMPANY: GILEAD SCIENCES

DESCRIPTION: Lipid spheres, called liposomes, which measure about 100 nanometers in diameter, encase an anticancer drug to treat the AIDS-related Kaposi's sarcoma.

APPLICATION: MANUFACTURE OF RAW MATERIALS

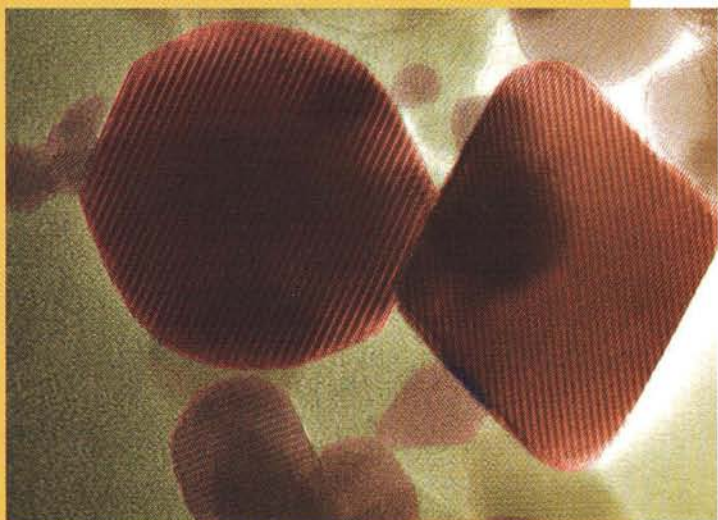
COMPANY: CARBON NANOTECHNOLOGIES

DESCRIPTION: Co-founded by buckyball discoverer Richard E. Smalley, the company has made carbon nanotubes more affordable by exploiting a new manufacturing process.

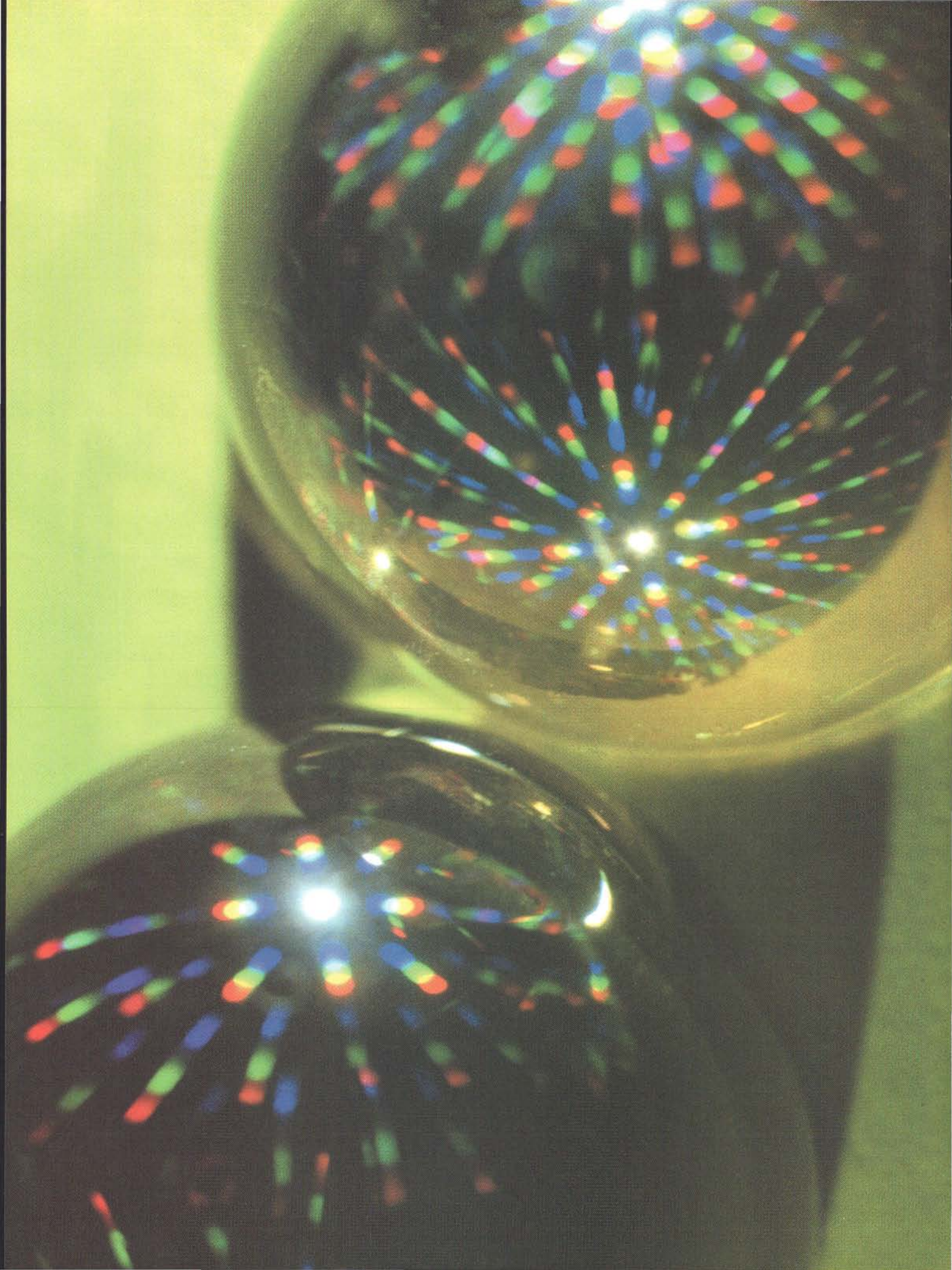
APPLICATION: MATERIALS ENHANCEMENT

COMPANY: NANOPHASE TECHNOLOGIES

DESCRIPTION: Nanocrystalline particles are incorporated into other materials to produce tougher ceramics, transparent sunblocks to block infrared and ultraviolet radiation, and catalysts for environmental uses, among other applications.



NANOPARTICLES are made by Nanophase Technologies.



The art of Building Small

BY GEORGE M. WHITESIDES
AND J. CHRISTOPHER LOVE

RESEARCHERS ARE DISCOVERING CHEAP,
EFFICIENT WAYS TO MAKE STRUCTURES
ONLY A FEW BILLIONTHS OF A METER ACROSS

INTRICATE DIFFRACTION PATTERNS are created by nanoscale-width rings (too small to see) on the surface of one-centimeter-wide hemispheres made of clear polymer. Kateri E. Paul, a graduate student in George M. Whitesides's group at Harvard University, fashioned the rings in a thin layer of gold on the hemispheres using a nanofabrication technique called soft lithography.

“Make it small!” is a technological edict that has changed the world. The development of microelectronics—first the transistor and then the aggregation of transistors into microprocessors, memory chips and controllers—has brought forth a cornucopia of machines that manipulate information by streaming electrons through silicon. Microelectronics rests on techniques that routinely fabricate structures almost as small as 100 nanometers across (that is, 100 billionths of a meter). This size is tiny by the standards of everyday experience—about one thousandth the width of a human hair—but it is large on the scale of atoms and molecules. The diameter of a 100-nanometer-wide wire would span about 500 atoms of silicon.

The idea of making “nanostructures” that comprise just one or a few atoms has great appeal, both as a scientific challenge and for practical reasons. A structure the size of an atom represents a fundamental limit: to make anything smaller would require manipulating atomic nuclei—essentially, transmuting one chemical element into another. In recent years, scientists have learned various techniques for building nanostructures, but they have only just begun to

investigate their properties and potential applications. The age of nanofabrication is here, and the age of nanoscience has dawned, but the age of nanotechnology—finding practical uses for nanostructures—has not really started yet.

The Conventional Approach

RESEARCHERS may well develop nanostructures as electronic components, but the most important applications could be quite different: for example, biologists might use nanometer-scale particles as minuscule sensors to investigate cells. Because scientists do not know what kinds of nanostructures they will ultimately want to build, they have not yet determined the best ways to construct them. Photolithography, the technology used to manufacture computer chips and virtually all other microelectronic systems, can be refined to make structures smaller than 100 nanometers, but doing so is very difficult, expensive and inconvenient. In a search to find better alternatives, nanofabrication researchers have adopted the philosophy “Let a thousand flowers bloom.”

First, consider the advantages and disadvantages of photolithography. Manufacturers use this phenomenally productive technology to churn out three bil-

lion transistors *per second* in the U.S. alone. Photolithography is basically an extension of photography. One first makes the equivalent of a photographic negative containing the pattern required for some part of a microchip’s circuitry. This negative, which is called the mask or master, is then used to copy the pattern into the metals and semiconductors of a microchip. As is the case with photography, the negative may be hard to make, but creating multiple copies is easy, because the mask can be used many times. The process thus separates into two stages: the preparation of the mask (a one-time event, which can be slow and expensive) and the use of the mask to manufacture replicas (which must be rapid and inexpensive).

To make a mask for a part of a computer chip, a manufacturer first designs the circuitry pattern on a conveniently large scale and converts it into a pattern of opaque metallic film (usually chromium) on a transparent plate (usually glass or silica). Photolithography then reduces the size of the pattern in a process analogous to that used in a photographic darkroom [see illustration on opposite page]. A beam of light (typically ultraviolet light from a mercury arc lamp) shines through the chromium mask, then passes through a lens that focuses the image onto a photosensitive coating of organic polymer (called the photoresist) on the surface of a silicon wafer. The parts of the photoresist struck by the light can be selectively removed, exposing parts of the silicon wafer in a way that replicates the original pattern.

Why not use photolithography to make nanostructures? The technology faces two limitations. The first is that the shortest wavelength of ultraviolet light currently used in production processes is about 250 nanometers. Trying to make structures much smaller than half of that spacing is like trying to read print that is

Overview/Nanofabrication

- The development of nanotechnology will depend on the ability of researchers to efficiently manufacture structures smaller than 100 nanometers (100 billionths of a meter) across.
- Photolithography, the technology now used to fabricate circuits on microchips, can be modified to produce nanometer-scale structures, but the modifications would be technically difficult and hugely expensive.
- Nanofabrication methods can be divided into two categories: top-down methods, which carve out or add aggregates of molecules to a surface, and bottom-up methods, which assemble atoms or molecules into nanostructures.
- Two examples of promising top-down methods are soft lithography and dip-pen lithography. Researchers are using bottom-up methods to produce quantum dots that can serve as biological dyes.

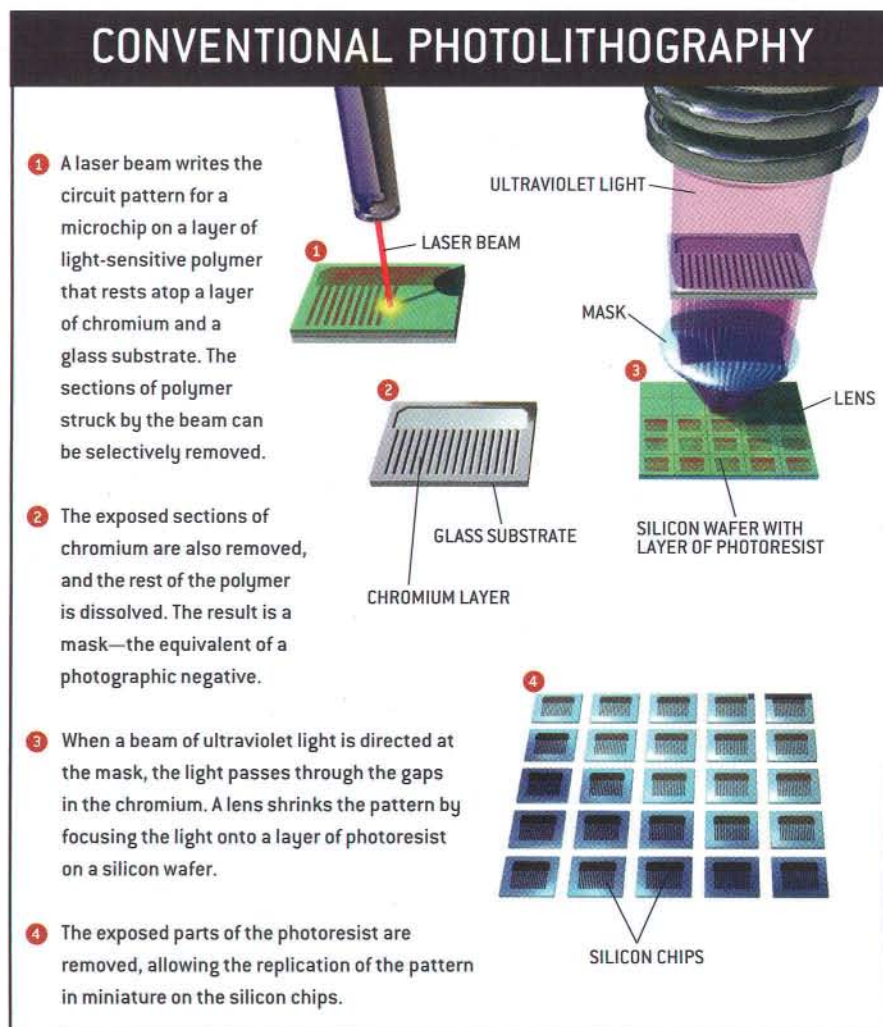
too tiny: diffraction causes the features to blur and meld together. Various technical improvements have made it possible to push the limits of photolithography. The smallest structures created in mass production are somewhat larger than 100 nanometers, and complex micro-electronic structures have been made with features that are only 70 nanometers across. But these structures are still not small enough to explore some of the most interesting aspects of nanoscience.

The second limitation follows from the first: because it is technically difficult to make such small structures using light, it is also very expensive to do so. The photolithographic tools that will be used to make chips with features well below 100 nanometers will each cost tens to hundreds of millions of dollars. This expense may or may not be acceptable to manufacturers, but it is prohibitive for the biologists, materials scientists, chemists and physicists who wish to explore nanoscience using structures of their own design.

Future Nanochips

THE ELECTRONICS industry is deeply interested in developing new methods for nanofabrication so that it can continue its long-term trend of building ever smaller, faster and less expensive devices. It would be a natural evolution of microelectronics to become nanoelectronics. But because conventional photolithography becomes more difficult as the dimensions of the structures become smaller, manufacturers are exploring alternative technologies for making future nanochips.

One leading contender is electron-beam lithography. In this method, the circuitry pattern is written on a thin polymer film with a beam of electrons. An electron beam does not diffract at atomic scales, so it does not cause blurring of the edges of features. Researchers have used the technique to write lines with widths of only a few nanometers in a layer of photoresist on a silicon substrate. The electron-beam instruments currently available, however, are very expensive and impractical for large-scale manufacturing. Because the beam of electrons is needed to fabricate each structure, the process is similar to the copying of a



manuscript by hand, one line at a time.

If electrons are not the answer, what is? Another contender is lithography using x-rays with wavelengths between 0.1 and 10 nanometers or extreme ultraviolet light with wavelengths between 10 and 70 nanometers. Because these forms of radiation have much shorter wavelengths than the ultraviolet light currently used in photolithography, they minimize the blurring caused by diffraction. These technologies face their own set of problems, however: conventional lenses are not transparent to extreme ultraviolet light and do not focus x-rays. Furthermore, the energetic radiation rapid-

ly damages many of the materials used in masks and lenses. But the microelectronics industry clearly would prefer to make advanced chips using extensions of familiar technology, so these methods are being actively developed. Some of the techniques (for example, advanced ultraviolet lithography for chip production) will probably become commercial realities. They will not, though, make inexpensive nanostructures and thus will do nothing to open nanotechnology to a broader group of scientists and engineers.

The need for simpler and less expensive methods of fabricating nanostructures has stimulated the search for un-

THE AUTHORS

GEORGE M. WHITESIDES and J. CHRISTOPHER LOVE work together on unconventional methods of nanofabrication in the department of chemistry at Harvard University. Whitesides, a professor of chemistry, received his Ph.D. from the California Institute of Technology in 1964 and joined the Harvard faculty in 1982. Love is a graduate student and a member of Whitesides's research group. He received his bachelor's degree in chemistry from the University of Virginia in 1999 and his master's degree from Harvard in 2001.

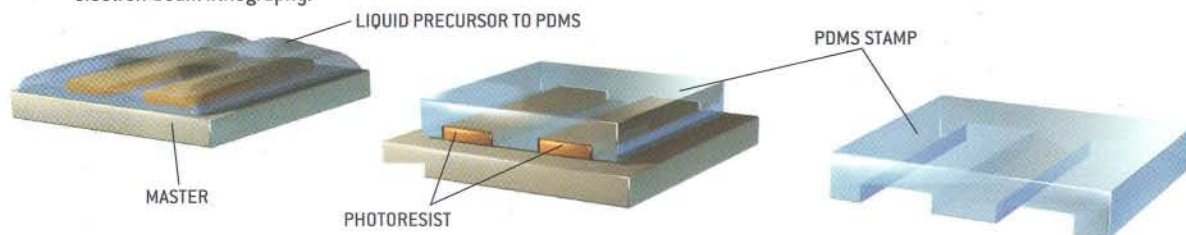
SOFT LITHOGRAPHY

Printing, molding and other mechanical processes carried out using an elastic stamp can produce patterns with nanoscale features.

Such techniques can fabricate devices that might be used in optical communications or biochemical research.

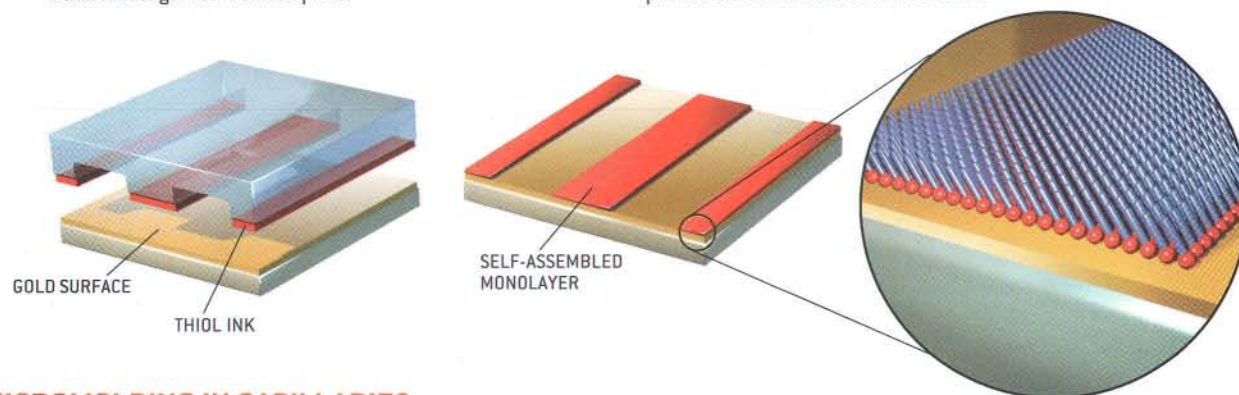
MAKING AN ELASTIC STAMP

- 1 A liquid precursor to polydimethylsiloxane (PDMS) is poured over a bas-relief master produced by photolithography or electron-beam lithography.
- 2 The liquid is cured into a rubbery solid that matches the original pattern.
- 3 The PDMS stamp is peeled off the master.



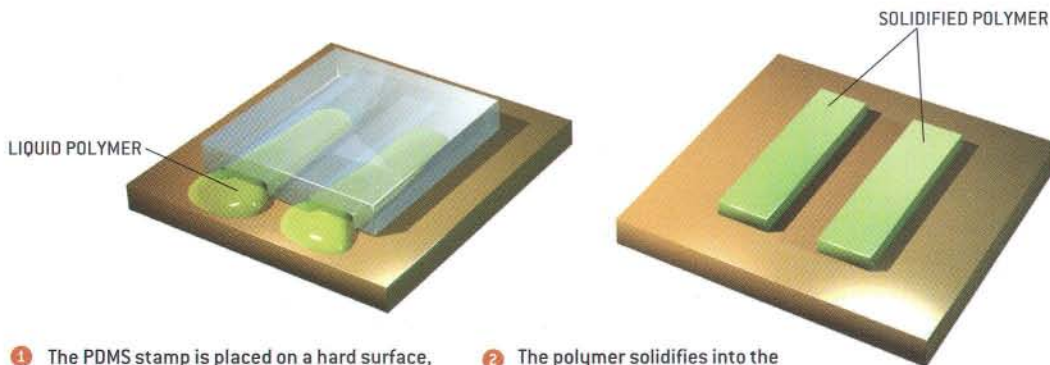
MICROCONTACT PRINTING

- 1 The PDMS stamp is inked with a solution consisting of organic molecules called thiols and then pressed against a thin film of gold on a silicon plate.
- 2 The thiols form a self-assembled monolayer on the gold surface that reproduces the stamp's pattern; features in the pattern are as small as 50 nanometers.



MICROMOLDING IN CAPILLARIES

- 1 The PDMS stamp is placed on a hard surface, and a liquid polymer flows into the recesses between the surface and the stamp.
- 2 The polymer solidifies into the desired pattern, which may contain features smaller than 10 nanometers.



conventional approaches that have not been explored by the electronics industry. We first became interested in the topic in the 1990s when we were engaged in making the simple structures required in microfluidic systems—chips with channels and chambers for holding liquids. This lab-on-a-chip has myriad potential uses in biochemistry, ranging from drug screening to genetic analysis. The channels in microfluidic chips are enormous by the standards of microelectronics: 50 microns (or 50,000 nanometers) wide, rather than 100 nanometers. But the techniques for producing those channels are quite versatile. Microfluidic chips can be made quickly and inexpensively, and many are composed of organic polymers and gels—materials not found in the world of electronics. We discovered that

matches the original pattern with astonishing fidelity: the stamp reproduces features from the master as small as a few nanometers. Although the creation of a finely detailed bas-relief master is expensive because it requires electron-beam lithography or other advanced techniques, copying the pattern on PDMS stamps is cheap and easy. And once a stamp is in hand, it can be used in various inexpensive ways to make nanostructures.

The first method—originally developed by Amit Kumar, a postdoctoral student in our group at Harvard University—is called microcontact printing. The PDMS stamp is “inked” with a reagent solution consisting of organic molecules called thiols [see *middle illustration on opposite page*]. The stamp is then brought into contact with an appropriate sheet of

are in the field of nanofluidics, an extension of microfluidics that would involve producing chips for biochemical research with channels only a few nanometers wide. At that scale, fluid dynamics may allow new ways to separate materials such as fragments of DNA.

These methods require no special equipment and in fact can be carried out by hand in an ordinary laboratory. Conventional photolithography must take place in a clean-room facility devoid of dust and dirt; if a piece of dust lands on the mask, it will create an unwanted spot on the pattern. As a result, the device being fabricated (and sometimes neighboring devices) may fail. Soft lithography is generally more forgiving because the PDMS stamp is elastic. If a piece of dust gets trapped between the stamp and the sur-

These methods require no special equipment and in fact can be carried out by hand in an ordinary lab.

we could use similar techniques to create nanostructures.

The methods represented, in a sense, a step backward in technology. Instead of using the tools of physics—light and electrons—we employed mechanical processes that are familiar in everyday life: printing, stamping, molding and embossing. The techniques are called soft lithography because the tool they have in common is a block of polydimethylsiloxane (PDMS)—the rubbery polymer used to caulk the leaks around bathtubs. (Physicists often refer to such organic chemicals as “soft matter.”)

To carry out reproduction using soft lithography, one first makes a mold or a stamp. The most prevalent procedure is to use photolithography or electron-beam lithography to produce a pattern in a layer of photoresist on the surface of a silicon wafer. This process generates a bas-relief master in which islands of photoresist stand out from the silicon [see *top illustration on opposite page*]. Then a chemical precursor to PDMS—a free-flowing liquid—is poured over the bas-relief master and cured into the rubbery solid. The result is a PDMS stamp that

“paper”—a thin film of gold on a glass, silicon or polymer plate. The thiols react with the gold surface, forming a highly ordered film (called a self-assembled monolayer, or SAM) that replicates the stamp’s pattern. Because the thiol ink spreads a bit after it contacts the surface, the resolution of the monolayer cannot be quite as high as that of the PDMS stamp. But when used correctly, microcontact printing can produce patterns with features as small as 50 nanometers.

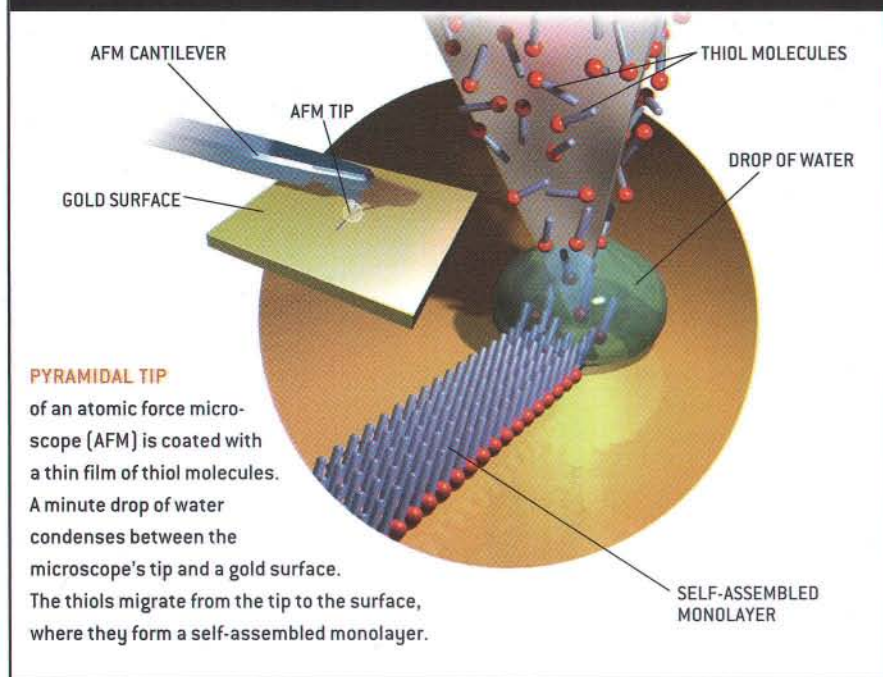
Another method of soft lithography, called micromolding in capillaries, involves using the PDMS stamp to mold patterns. The stamp is placed on a hard surface, and a liquid polymer flows by capillary action into the recesses between the surface and the stamp [see *bottom illustration on opposite page*]. The polymer then solidifies into the desired pattern. This technique can replicate structures smaller than 10 nanometers. It is particularly well suited for producing subwavelength optical devices, waveguides and optical polarizers, all of which could be used in optical fiber networks and eventually perhaps in optical computers. Other possible applications

face, the stamp will compress over the top of the particle but maintain contact with the rest of the surface. Thus, the pattern will be reproduced correctly except for where the contaminant is trapped.

Moreover, soft lithography can produce nanostructures in a wide range of materials, including the complex organic molecules needed for biological studies. And the technique can print or mold patterns on curved as well as planar surfaces. But the technology is not ideal for making the structures required for complex nanoelectronics. Currently all integrated circuits consist of stacked layers of different materials. Deformations and distortions of the soft PDMS stamp can produce small errors in the replicated pattern and a misalignment of the pattern with any underlying patterns previously fabricated. Even the tiniest distortions or misalignments can destroy a multilayered nanoelectronic device. Therefore, soft lithography is not well suited for fabricating structures with multiple layers that must stack precisely on top of one another.

Researchers have found ways, however, to correct this shortcoming—at

DIP-PEN LITHOGRAPHY



least in part—by employing a rigid stamp instead of an elastic one. In a technique called step-and-flash imprint lithography, developed by C. Grant Willson of the University of Texas, photolithography is used to etch a pattern into a quartz plate, yielding a rigid bas-relief master. Willson eliminated the step of making a PDMS stamp from the master; instead the master itself is pressed against a thin film of liquid polymer, which fills the master's recesses. Then the master is exposed to ultraviolet light, which solidifies the polymer to create the desired replica. A related technique called nanoimprint lithography, developed by Stephen Y. Chou of Princeton University, also employs a rigid master but uses a film of polymer that has been heated to a temperature near its melting point to facilitate the embossing process. Both methods can produce two-dimensional structures with good fidelity, but it remains to be seen whether the techniques are suitable for manufacturing electronic devices.

Pushing Atoms Around

THE CURRENT REVOLUTION in nanoscience started in 1981 with the invention of the scanning tunneling microscope (STM), for which Heinrich Rohrer and Gerd K. Binnig of the IBM Zurich

Research Laboratory received the Nobel Prize in Physics in 1986. This remarkable device detects small currents that pass between the microscope's tip and the sample being observed, allowing researchers to "see" substances at the scale of individual atoms. The success of the STM led to the development of other scanning probe devices, including the atomic force microscope (AFM). The operating principle of the AFM is similar to that of an old-fashioned phonograph. A tiny probe—a fiber or a pyramid-shaped tip that is typically between two and 30 nanometers wide—is brought into direct contact with the sample. The probe is attached to the end of a cantilever, which bends as the tip moves across the sample's surface. The deflection is measured by reflecting a beam of laser light off the top of the cantilever. The AFM can detect variations in vertical surface topography that are smaller than the dimensions of the probe.

But scanning probe devices can do more than simply allow scientists to observe the atomic world—they can also be used to create nanostructures. The tip on the AFM can be used to physically move nanoparticles around on surfaces and to arrange them in patterns. It can also be used to make scratches in a surface (or

more commonly, in monolayer films of atoms or molecules that coat the surface). Similarly, if researchers increase the currents flowing from the tip of the STM, the microscope becomes a very small source for an electron beam, which can be used to write nanometer-scale patterns. The STM tip can also push individual atoms around on a surface to build rings and wires that are only one atom wide.

An intriguing new scanning probe fabrication method is called dip-pen lithography. Developed by Chad A. Mirkin of Northwestern University, this technique works much like a goose-feather pen [see illustration at left]. The tip of the AFM is coated with a thin film of thiol molecules that are insoluble in water but react with a gold surface (the same chemistry used in microcontact printing). When the device is placed in an atmosphere containing a high concentration of water vapor, a minute drop of water condenses between the gold surface and the microscope's tip. Surface tension pulls the tip to a fixed distance from the gold, and this distance does not change as the tip moves across the surface. The drop of water acts as a bridge over which the thiol molecules migrate from the tip to the gold surface, where they are fixed. Researchers have used this procedure to write lines a few nanometers across.

Although dip-pen lithography is relatively slow, it can use many different types of molecules as "inks" and thus brings great chemical flexibility to nanometer-scale writing. Researchers have not yet determined the best applications for the technique, but one idea is to use the dip-pen method for precise modifications of circuit designs. Mirkin has recently demonstrated that a variant of the ink used in dip-pen lithography can write directly on silicon.

An interesting cousin to these techniques involves another kind of nanostructure, called a break junction. If you break a thin, ductile metal wire into two parts by pulling sharply, the process seems abrupt to a human observer, but it actually follows a complex sequence. When the force used in breaking the wire is first applied, the metal begins to yield and flow, and the diameter of the wire

decreases. As the two ends move apart, the wire gets thinner and thinner until, in the instant just before breaking, it is a single atom in diameter at its narrowest point. This process of thinning a wire to a break junction can be detected easily by measuring the current that flows through the wire. When the wire is slender enough, current can flow only in discrete quantities (that is, current flow is quantized).

The break junction is analogous to two STM tips facing each other, and similar physical rules govern the current that flows through it. Mark A. Reed of Yale University has pioneered a particularly inventive use of the break junction. He built a device that enabled a thin junction to be broken under carefully controlled conditions and then allowed the broken tips to be brought back together or to be held apart at any distance with an accuracy of a few thousandths of a nanometer. By adjusting the distance between the tips in the presence of an organic molecule that bridged them, Reed was able to measure a current flowing across the organic bridge. This experiment was an important step in the development of technolo-

gies for using single organic molecules as electronic devices such as diodes and transistors [see "Computing with Molecules," by Mark A. Reed and James M. Tour; *SCIENTIFIC AMERICAN*, June 2000].

Top-Down and Bottom-Up

ALL THE FORMS of lithography we have discussed so far are called top-down methods—that is, they begin with a pattern generated on a larger scale and reduce its lateral dimensions (often by a factor of 10) before carving out nanostructures. This strategy is required in fabricating electronic devices such as microchips, whose functions depend more on their patterns than on their dimensions. But no top-down method is ideal; none can conveniently, cheaply and quickly make nanostructures of any material. So researchers have shown growing interest in bottom-up methods, which start with atoms or molecules and build *up* to nanostructures. These methods can easily make the smallest nanostructures—with dimensions between two and 10 nanometers—and do so inexpensively. But these structures are usu-

ally generated as simple particles in suspension or on surfaces, rather than as designed, interconnected patterns.

Two of the most prominent bottom-up methods are those used to make nanotubes and quantum dots. Scientists have made long, cylindrical tubes of carbon by a catalytic growth process that employs a nanometer-scale drop of molten metal (usually iron) as a catalyst [see "Nanotubes for Electronics," by Philip G. Collins and Phaedon Avouris; *SCIENTIFIC AMERICAN*, December 2000]. The most active area of research in quantum dots originated in the laboratory of Louis E. Brus (then at Bell Laboratories) and has been developed by A. Paul Alivisatos of the University of California at Berkeley, Moungi G. Bawendi of the Massachusetts Institute of Technology, and others. Quantum dots are crystals containing only a few hundred atoms. Because the electrons in a quantum dot are confined to widely separated energy levels, the dot emits only one wavelength of light when it is excited. This property makes the quantum dot useful as a biological marker [see

Nanofabrication: Comparing the Methods

Researchers are developing an array of techniques for building structures smaller than 100 nanometers. Here is a summary of the advantages and disadvantages of four methods.

Photolithography

Advantages: The electronics industry is already familiar with this technology because it is currently used to fabricate microchips. Manufacturers can modify the technique to produce nanometer-scale structures by employing electron beams, x-rays or extreme ultraviolet light.

Disadvantages: The necessary modifications will be expensive and technically difficult. Using electron beams to fashion structures is costly and slow. X-rays and extreme ultraviolet light can damage the equipment used in the process.

Scanning Probe Methods

Advantages: The scanning tunneling microscope and the atomic force microscope can be used to move individual nanoparticles and arrange them in patterns. The instruments can build rings and wires that are only one atom wide.

Disadvantages: The methods are too slow for mass production. Applications of the microscopes will probably be limited to the fabrication of specialized devices.

Soft Lithography

Advantages: This method allows researchers to inexpensively reproduce patterns created by electron-beam lithography or other related techniques. Soft lithography requires no special equipment and can be carried out by hand in an ordinary laboratory.

Disadvantages: The technique is not ideal for manufacturing the multilayered structures of electronic devices. Researchers are trying to overcome this drawback, but it remains to be seen whether these efforts will be successful.

Bottom-Up Methods

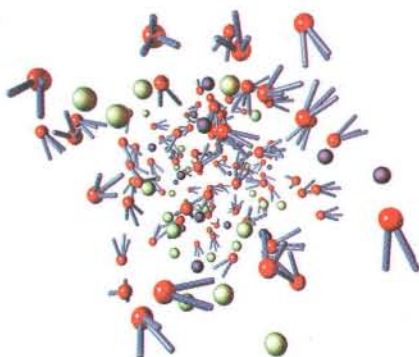
Advantages: By setting up carefully controlled chemical reactions, researchers can cheaply and easily assemble atoms and molecules into the smallest nanostructures, with dimensions between two and 10 nanometers.

Disadvantages: Because these methods cannot produce designed, interconnected patterns, they are not well suited for building electronic devices such as microchips.

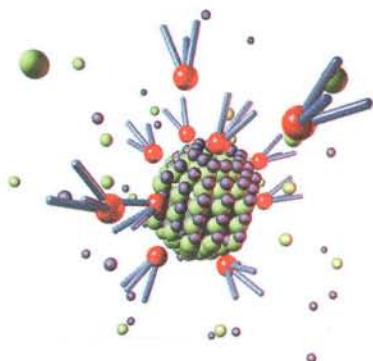
QUANTUM DOT ASSEMBLY

Crystals called quantum dots contain only a few hundred atoms and emit different wavelengths of light, depending on their size. They may become useful as biological markers of cellular activity.

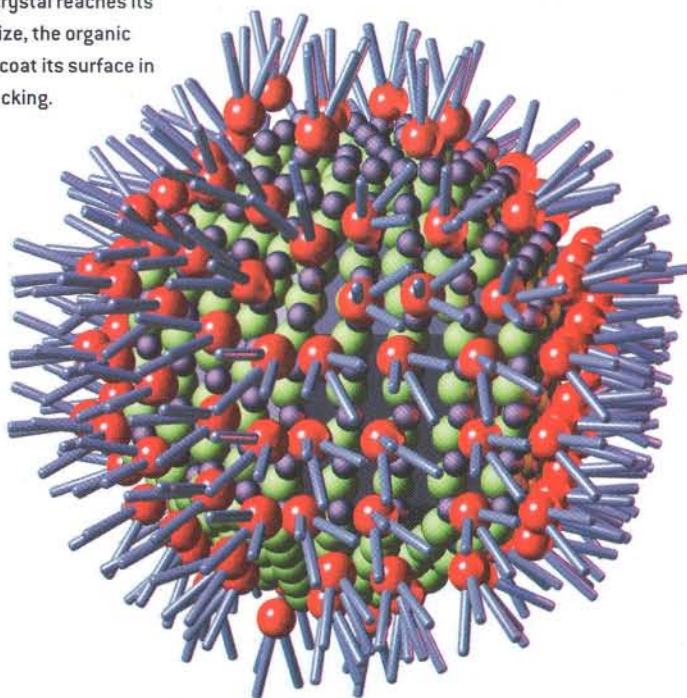
- 1 A chemical reaction brings together cadmium ions (purple), selenium ions (green) and organic molecules (red spheres with blue tails).



- 2 The organic molecules act as surfactants, binding to the surface of the cadmium selenide crystal as it grows.



- 3 When the crystal reaches its optimum size, the organic molecules coat its surface in a stable packing.



"Less Is More in Medicine," on page 58].

One procedure used to make quantum dots involves a chemical reaction between a metal ion (for example, cadmium) and a molecule that is able to donate a selenium ion. This reaction generates crystals of cadmium selenide. The trick is to prevent the small crystals from sticking together as they grow to the desired size. To insulate the growing particles from one another, researchers carry out the reaction in the presence of organic molecules that act as surfactants, coating the surface of each cadmium selenide particle as it grows. The organic molecules stop the crystals from clumping together and regulate their rate of growth. The geometry of the particles can be controlled to some extent by mixing different ratios of the organic molecules. The reaction can generate particles with a variety of shapes, including spheres, rods and tetrapods (four-armed particles similar to toy jacks).

It is important to synthesize the quantum dots with uniform size and composition, because the size of the dot determines its electronic, magnetic and optical properties. Researchers can select the size of the particles by varying the length of time for the reaction. The organic coating also helps to set the size of the particles. When the nanoparticle is small (on the scale of molecules), the organic coating is loose and allows further growth; as the particle enlarges, the organic molecules become crowded. There is an optimum size for the particles that allows the most stable packing of the organic molecules and thus provides the greatest stabilization for the surfaces of the crystals.

These cadmium selenide nanoparticles promise some of the first commercial products of nanoscience: Quantum Dot Corporation has been developing the crystals for use as biological labels. Researchers can tag proteins and nucleic acids with quantum dots; when the sample is illuminated with ultraviolet light, the crystals will fluoresce at a specific wavelength and thus show the locations of the attached proteins. Many organic molecules also fluoresce, but quantum dots have several advantages that make them better markers. First, the color of

a quantum dot's fluorescence can be tailored by changing the dot's size: the larger the particle, the more the emitted light is shifted toward the red end of the spectrum. Second, if all the dots are the same size, their fluorescence spectrum is narrow—that is, they emit a very pure color. This property is important because it allows particles of different sizes to be used as distinguishable labels. Third, the fluorescence of quantum dots does not fade on exposure to ultraviolet light, as does that of organic molecules. When used as dyes in biological research, the dots can be observed for conveniently long periods.

Scientists are also investigating the possibility of making structures from colloids—nanoparticles in suspension. Christopher B. Murray and a team at the IBM Thomas J. Watson Research Center are exploring the use of such colloids to create a medium for ultrahigh-density data storage. The IBM team's colloids contain magnetic nanoparticles as small as

mammalian cells are larger. Cells are, however, filled with much smaller structures, many of which are astonishingly sophisticated. The ribosome, for example, carries out one of the most important cellular functions: the synthesis of proteins from amino acids, using messenger RNA as the template. The complexity of this molecular construction project far surpasses that of man-made techniques. Or consider the rotary motors of the bacterial flagella, which efficiently propel the one-celled organisms [see "The Once and Future Nanomachine," on page 70].

It is unclear if "nanomachines" taken from cells will be useful. They will probably have very limited application in electronics, but they may provide valuable tools for chemical synthesis and sensing devices. Recent work by Carlo D. Montemagno of Cornell University has shown that it is possible to engineer a primitive nanomachine with a biological engine. Montemagno extracted a rotary motor protein from a bacterial cell and

The development of nanotechnology will depend on the availability of nanostructures. The invention of the STM and AFM has provided new tools for viewing, characterizing and manipulating these structures; the issue now is how to build them to order and how to design them to have new and useful functions. The importance of electronics applications has tended to focus attention on nanodevices that might be incorporated into future integrated circuits. And for good technological reasons, the electronics industry has emphasized fabrication methods that are extensions of those currently used to make microchips. But the explosion of interest in nanoscience has created a demand for a broad range of fabrication methods, with an emphasis on low-cost, convenient techniques.

The new approaches to nanofabrication are unconventional only because they are not derived from the microtechnology developed for electronic devices.

Bottom-up methods start from atoms or molecules and build up to nanostructures.

three nanometers across, each composed of about 1,000 iron and platinum atoms. When the colloid is spread on a surface and the solvent allowed to evaporate, the nanoparticles crystallize in two- or three-dimensional arrays. Initial studies indicate that these arrays can potentially store trillions of bits of data per square inch, giving them a capacity 10 to 100 times greater than that of present memory devices.

The Future of Nanofabrication

THE INTEREST in nanostructures is so great that every plausible fabrication technique is being examined. Although physicists and chemists are now doing most of the work, biologists may also make important contributions. The cell (whether mammalian or bacterial) is relatively large on the scale of nanostructures: the typical bacterium is approximately 1,000 nanometers long, and

connected it to a metallic nanorod—a cylinder 750 nanometers long and 150 nanometers wide that had been fabricated by lithography. The rotary motor, which was only 11 nanometers tall, was powered by adenosine triphosphate (ATP), the source of chemical energy in cells. Montemagno showed that the motor could rotate the nanorod at eight revolutions per minute. At the very least, such research stimulates efforts to fabricate functional nanostructures by demonstrating that such structures can exist.

Chemists, physicists and biologists are rapidly accepting these techniques as the most appropriate ways to build various kinds of nanostructures for research. And the methods may even supplement the conventional approaches—photolithography, electron-beam lithography and related techniques—for applications in electronics as well. The microelectronics mold is now broken. Ideas for nanofabrication are coming from many directions in a wonderful free-for-all of discovery.

MORE TO EXPLORE

More information about nanofabrication can be found at the following Web sites:

International SEMATECH: www.sematech.org/public/index.htm

The Whitesides group at Harvard University: gmwgroup.harvard.edu

The Mirkin group at Northwestern University: www.chem.northwestern.edu/~mkngpr/

The Willson group at the University of Texas at Austin: willson.cm.utexas.edu/Research/research.htm

The Alivisatos group at the University of California at Berkeley: www.cchem.berkeley.edu/~pagrp/

The Bawendi group at M.I.T.: web.mit.edu/chemistry/nanocluster/

The Montemagno group at Cornell University: falcon.aben.cornell.edu/

Plenty of Room, Indeed

There is plenty of room for practical innovation at the nanoscale. But first, scientists have to understand the unique physics that governs matter there

By Michael Roukes

Back in December 1959, future Nobel laureate Richard Feynman gave a visionary and now oft-quoted talk entitled "There's Plenty of Room at the Bottom." The occasion was an American Physical Society meeting at the California Institute of Technology, Feynman's intellectual home then and mine today. Although he didn't intend it, Feynman's 7,000 words were a defining moment in nanotechnology, long before anything "nano" appeared on the horizon.

"What I want to talk about," he said, "is the problem of manipulating and controlling things on a small scale.... What I have demonstrated is that there is room—that you can decrease the size of things in a practical way. I now want to show that there is

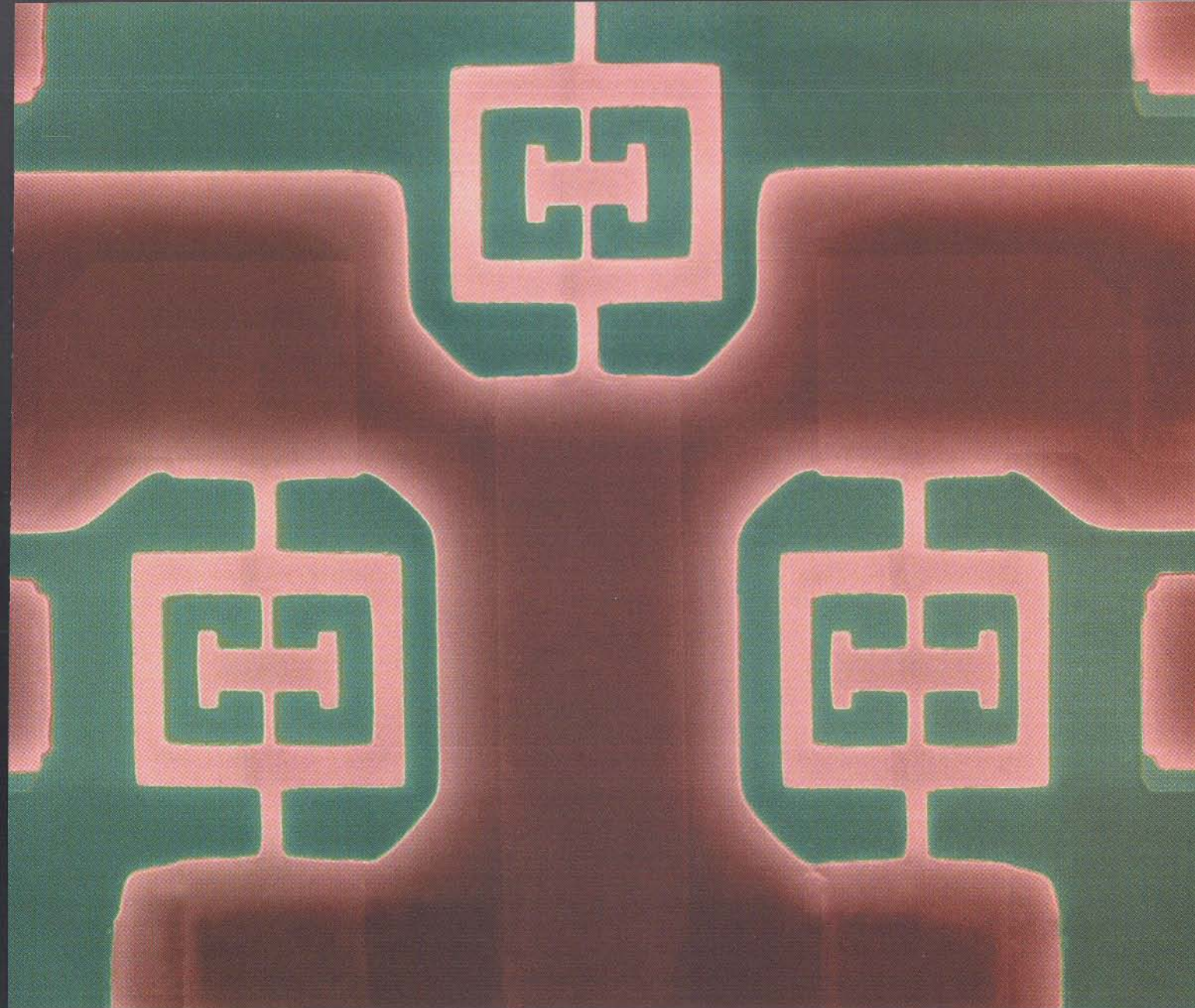
plenty of room. *I will not now discuss how we are going to do it, but only what is possible in principle.... We are not doing it simply because we haven't yet gotten around to it.*"

The breadth of Feynman's vision is staggering. In that lecture 42 years ago he anticipated a spectrum of scientific and technical fields that are now well established, among them electron-beam and ion-beam fabrication, molecular-beam epitaxy, nanoimprint lithography, projection electron microscopy, atom-by-atom manipulation, quantum-effect electronics, spin electronics (also called spintronics) and microelectromechanical systems (MEMS). The lecture also projected what has been called the "magic" Feynman brought to everything he turned

his singular intellect toward. Indeed, it has profoundly inspired my two decades of research on physics at the nanoscale.

Today there is a nanotechnology gold rush. Nearly every major funding agency for science and engineering has announced its own thrust into the field. Scores of researchers and institutions are scrambling for a piece of the action. But in all honesty, I think we have to admit that much of what invokes the hallowed prefix "nano" falls a bit short of Feynman's mark.

We've only just begun to take the first steps toward his grand vision of assembling complex machines and circuits atom by atom. What can be done now is extremely rudimentary. We're certainly nowhere near being able to commercial-



ly mass-produce nanosystems—integrated multicomponent nanodevices that have the complexity and range of functions readily provided by modern microchips. But there is a fundamental science issue here as well. It is becoming increasingly clear that we are only *beginning* to acquire the detailed knowledge that will be at the heart of future nanotechnology. This new science concerns the properties and behavior of aggregates of atoms and molecules, at a scale not yet large enough to be considered macroscopic but far beyond what can be called microscopic. It is the science of the *meso-scale*, and until we understand it, practical devices will be difficult to realize.

Today's scientists and engineers readily fashion nanostructures on a scale

NOVEL NANOTECH DEVICES, such as these nanoelectromechanical resonators, are enabling scientists to discover the laws of physics that regulate the unique properties of matter at the mesoscale.

of one to a few hundred nanometers—small indeed, but much bigger than simple molecules. Matter at this mesoscale is often awkward to explore. It contains too many atoms to be easily understood by straightforward application of quantum mechanics (although the fundamental laws still apply). Yet these systems are not so large as to be completely free of quantum effects; thus, they do not simply obey the classical physics governing the macroworld. It is precisely in this intermediate domain, the mesoworld, that unforeseen properties of collective systems emerge.

Researchers are approaching this

transitional frontier using complementary top-down and bottom-up fabrication methods. Advances in top-down nanofabrication techniques such as electron-beam lithography (used extensively by my own research group) yield almost atomic-scale precision, but achieving success, not to mention reproducibility, as we scale down to the single-digit-nanometer regime becomes problematic. Alternatively, scientists are using bottom-up techniques for *self-assembly* of atoms. But the advent of preprogrammed self-assembly of arbitrarily large systems—with complexity comparable to that built every day in microelectronics, in

It is becoming increasingly clear that we are only beginning to acquire the detailed knowledge that will be at the heart of future nanotechnology.

MEMS and (of course) by Mother Nature—is nowhere on the horizon. It appears that the top-down approach will most likely remain the method of choice for building really complex devices for a good while (for more, see “The Art of Building Small,” on page 32).

Our difficulty in approaching the mesoscale from above or below bespeaks a basic challenge of physics. Lately, the essence of Feynman’s “Plenty of Room” talk seems to be taken as a license for *laissez faire* in nanotechnology. Yet Feynman never asserted that “anything goes” at the nanoscale. He warned, for instance, that the very act of trying to “*arrange the atoms one by one the way we want them*” is subject to fundamental principles: “*You can’t put them so that they are chemically unstable, for example.*” Accordingly, today’s scanning probe microscopes can move atoms from place to place on a prepared surface, but this ability does not immediately confer the power to build complex molecular assemblies at will. What has been accomplished so far, though impressive, is still quite limited. We will ultimately develop operational procedures to help us coax the formation of individual atomic bonds under more general conditions. But as we try to assemble complex networks of these bonds, they certainly will affect one

another in ways we do not yet understand and, hence, cannot yet control.

Feynman’s original vision was clearly intended to be inspirational. Were he observing now, he would surely be alarmed when people take his projections as some sort of gospel. He delivered his musings with characteristic playfulness as well as deep insight. Sadly for us, the field that would be called nanotechnology was just one of many that intrigued him. He never really continued with it, returning to give but one redux of his original lecture, at the Jet Propulsion Laboratory in 1983.

New Laws Prevail

IN 1959, and even in 1983, the complete physical picture of the nanoscale was far from clear. The good news for researchers is that, by and large, it still is! Much exotic territory awaits exploration. As we delve into it, we will uncover a panoply of phenomena that we must understand before practical nanotechnology will become possible. The past two decades have seen the elucidation of entirely new, fundamental physical principles that govern behavior at the mesoscale. Let’s consider three important examples.

In the fall of 1987 graduate student Bart J. van Wees of the Delft University

of Technology and Henk van Houten of the Philips Research Laboratories (both in the Netherlands) and collaborators were studying the flow of electric current through what are now called quantum-point contacts. These are narrow conducting paths within a semiconductor, along which electrons are forced to flow [see illustration on page 46]. Late one evening van Wees’s undergraduate assistant, Leo Kouwenhoven, was measuring the conductance through the constriction as he varied its width systematically. The research team was expecting to see only subtle conductance effects against an otherwise smooth and unremarkable background response. Instead there appeared a very pronounced, and now characteristic, staircase pattern. Further analysis that night revealed that plateaus were occurring at regular, precise intervals.

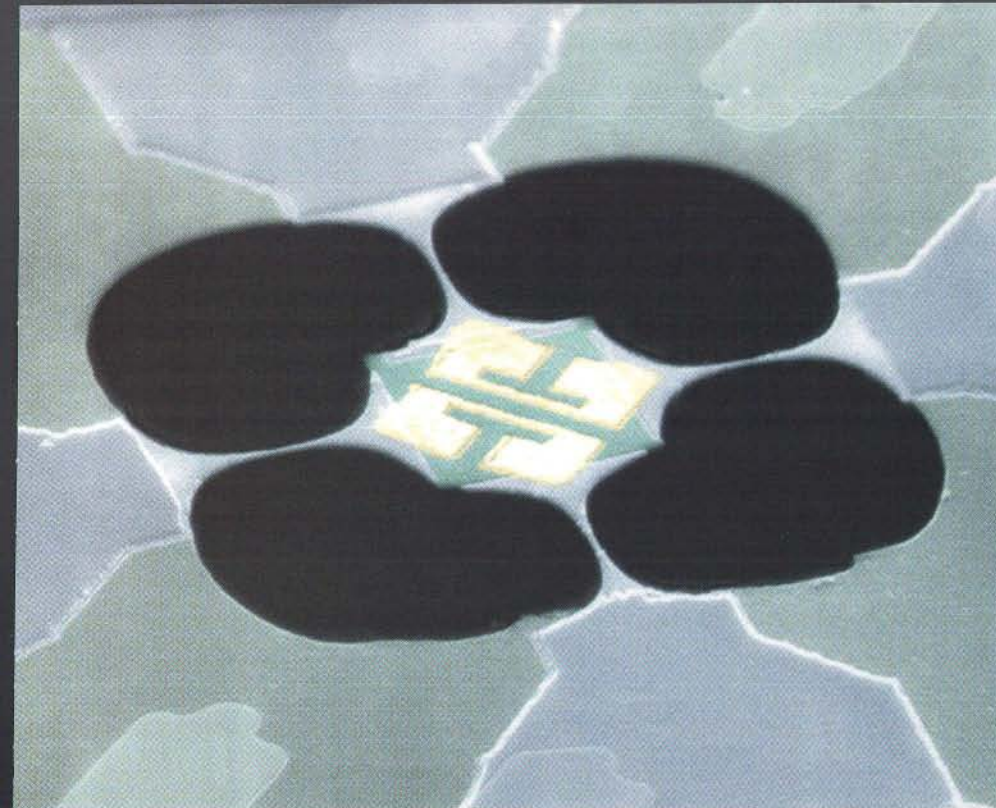
David Wharam and Michael Pepper of the University of Cambridge observed similar results. The two discoveries represented the first robust demonstrations of the *quantization of electrical conductance*. This is a basic property of small conductors that occurs when the wave-like properties of electrons are coherently maintained from the “source” to the “drain”—the input to the output—of a nanoelectronic device.

Feynman anticipated, in part, such odd behavior: “*I have thought about some of the problems of building electric circuits on a small scale, and the problem of resistance is serious....*” But the experimental discoveries pointed out something truly new and fundamental: quantum mechanics can completely govern the behavior of small electrical devices.

Direct manifestations of quantum mechanics in such devices were envisioned back in 1957 by Rolf Landauer, a theoretician at IBM who pioneered ideas in nanoscale electronics and in the physics of computation. But only in the mid-1980s did control over materials

Overview/Nanophysics

- Smaller than macroscopic objects but larger than molecules, nanotechnological devices exist in a unique realm—the mesoscale—where the properties of matter are governed by a complex and rich combination of classical physics and quantum mechanics.
- Engineers will not be able to make reliable or optimal nanodevices until they comprehend the physical principles that prevail at the mesoscale.
- Scientists are discovering mesoscale laws by fashioning unusual, complex systems of atoms and measuring their intriguing behavior.
- Once we understand the science underlying nanotechnology, we can fully realize the prescient vision of Richard Feynman: that nature has left plenty of room in the nanoworld to create practical devices that can help humankind.



NANOBIDGE DEVICE allowed Caltech physicists to first observe the quantization of thermal conductance—a fundamental limit to heat flow in minute objects. Four holes (black) etched into a silicon nitride membrane defined an isolated thermal reservoir (central green square) suspended by four narrow bridges. One gold transducer (yellow) electrically heated this reservoir; the second measured its temperature. Thin superconducting films (blue) on top of the bridges electrically connected the transducers to off-chip instrumentation but carried no heat. The reservoir therefore cooled only through the silicon nitride bridges, which were so narrow that they passed only the lowest-energy heat waves.

and nanofabrication begin to provide access to this regime in the laboratory. The 1987 discoveries heralded the heyday of “mesoscopia.”

A second important example of newly uncovered mesoscale laws that have led to nascent nanotechnology was first postulated in 1985 by Konstantin Likharev, a young physics professor at Moscow State University working with postdoctoral student Alexander Zorin and undergraduate Dmitri Averin. They anticipated that scientists would be able to control the movement of single electrons on and off a so-called coulomb island—a conductor weakly coupled to the rest of a nanocircuit. This could form the basis for an entirely new type of device, called a single-electron transistor. The physical effects that arise when putting a single electron on a coulomb island become increasingly robust as the island is scaled downward. In very small devices, these single-electron charging effects can completely dominate the current flow.

Such considerations are becoming increasingly important technologically.

Projections from the International Technology Roadmap for Semiconductors, prepared by long-range thinkers in the industry, indicate that by 2014 the minimum feature size for transistors in computer chips will decrease to 20 nanometers. At this dimension, each switching event will involve the equivalent of only about eight electrons. Designs that properly account for single-electron charging will become crucial.

By 1987 advances in nanofabrication allowed Theodore A. Fulton and Gerald J. Dolan of Bell Laboratories to construct the first single-electron transistor [see illustration on page 48]. The single-electron charging they observed, now called the coulomb blockade, has since been seen in a wide array of structures. As experimental devices get small-

er, the coulomb blockade phenomenon is becoming the rule, rather than the exception, in weakly coupled nanoscale devices. This is especially true in experiments in which electric currents are passed through individual molecules. These molecules can act like coulomb islands by virtue of their weak coupling to electrodes leading back to the macro-world. Using this effect to advantage and obtaining robust, reproducible coupling to small molecules (in ways that can actually be engineered) are among the important challenges in the new field of molecular electronics.

In 1990, against this backdrop, I was at Bell Communications Research studying electron transport in mesoscopic semiconductors. In a side project, my colleagues Larry Schiavone and Axel Scherer and I began developing techniques that we hoped would elucidate the quantum nature of *heat* flow. The work required much more sophisticated nanostructures than the planar devices used to investigate mesoscopic electronics. We needed freely suspended devices, structures possessing full three-dimensional relief. Ignorance was bliss; I had no idea the experiments would be so involved that they would take almost a decade to realize.

The first big strides were made after I moved to Caltech in 1992, in a collaboration with John Worlock of the University of Utah and two successive postdocs in my group. Thomas Tighe developed the methods and devices that generated the first direct measurements of heat flow in nanostructures. Subsequently, Keith Schwab revised the design of the suspended nanostructures and put in place ultrasensitive superconducting instrumentation to interrogate them at ultralow temperatures, where the effects could be seen most clearly.

In the late summer of 1999 Schwab finally began observing heat flow through

THE AUTHOR

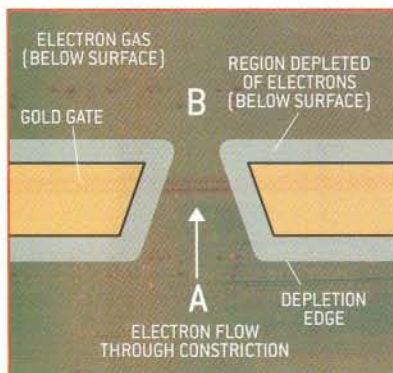
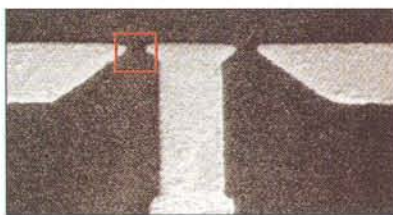
MICHAEL ROUKES, professor of physics at the California Institute of Technology, heads a group studying nanoscale systems. Among the holy grails his team is chasing are a potential billionfold improvement in present-day calorimetry, which would allow observation of the individual heat quanta being exchanged as nanodevices cool, and a potential quadrillion-fold increase in the sensitivity of magnetic resonance imaging, which would enable complex biomolecules to be visualized with three-dimensional atomic resolution.

ONE STEP AT A TIME

THE QUANTIZATION OF ELECTRICAL CONDUCTANCE

In 1987 Bart J. van Wees and his collaborators at the Delft University of Technology and Philips Research Laboratories (both in the Netherlands) built a novel structure (*micrograph*) that revealed a basic law governing nanotech circuits. Gold gate electrodes (*bright areas*) were placed atop a semiconductor substrate (*dark background*). Within the substrate, a planar sheet of charge carriers, called a two-dimensional electron gas, was created about 100 nanometers below the surface. The gates and the gas acted like the plates of a capacitor.

When a negative voltage bias was applied to the gates, electrons within the gas underneath the gates, and slightly beyond the gates' periphery, were pushed away. (The diagram shows this state.) When increasing negative voltage was applied, this "depletion edge" became more pronounced. At a certain threshold, carriers on either side of the constriction [between points A and B] became separated, and the conductance through the device was zero. From this threshold level, conductance did not resume smoothly. Instead it increased in stepwise fashion, where the steps occurred at values determined by twice the charge of the electron squared, divided by Planck's constant. This ratio is now called the electrical conductance quantum, and it indicates that electric current flows in nanocircuits at rates that are quantized.



silicon nitride nanobridges [see illustration on preceding page]. Even in these first data the fundamental limit to heat flow in mesoscopic structures emerged. The manifestation of this limit is now called the thermal conductance quantum. It determines the maximum rate at which heat can be carried by an individual wavelike mechanical vibration, spanning from the input to the output of a nanodevice. It is analogous to the electrical conductance quantum but governs the transport of heat.

This quantum is a significant parameter for nanoelectronics; it represents the ultimate limit for the power-dissipation problem. In brief, all "active" devices require a little energy to operate, and for them to operate stably without overheating, we must design a way to extract the heat they dissipate. As engineers try to ever increase the density of

transistors and the clock rates (frequencies) of microprocessors, the problem of keeping microchips cool to avoid complete system failure is becoming monumental. This will only become further exacerbated in nanotechnology.

Considering even this complexity, Feynman said, "Let the bearings run dry; they won't run hot because the heat escapes away from such a small device very, very rapidly." But our experiments indicate that nature is a little more restrictive. The thermal conductance quantum can place limits on how effectively a very small device can dissipate heat. What Feynman envisioned can be correct only if the nanoengineer designs a structure so as to take these limits into account.

From the three examples above, we can arrive at just one conclusion: we are only starting to unveil the complex and wonderfully different ways that nano-

scale systems behave. The discovery of the electrical and thermal conductance quanta and the observation of the coulomb blockade are true discontinuities—abrupt changes in our understanding. Today we are not accustomed to calling our discoveries "laws." Yet I have no doubt that electrical and thermal conductance quantization and single-electron-charging phenomena are indeed among the universal rules of nanodesign. They are new laws of the nanoworld. They do not contravene but augment and clarify some of Feynman's original vision. Indeed, he seemed to have anticipated their emergence: "At the atomic level, we have new kinds of forces and new kinds of possibilities, new kinds of effects. The problems of manufacture and reproduction of materials will be quite different."

We will encounter many more such discontinuities on the path to true nanotechnology. These welcome windfalls will occur in direct synchrony with advances in our ability to observe, probe and control nanoscale structures. It would seem wise, therefore, to be rather modest and circumspect about forecasting nanotechnology.

The Boon and Bane of Nano

THE NANOWORLD is often portrayed by novelists, futurists and the popular press as a place of infinite possibilities. But as you've been reading, this domain is not some ultraminiature version of the Wild West. *Not* everything goes down there; there are *laws*. Two concrete illustrations come from the field of nanoelectromechanical systems (NEMS), in which I am currently active.

Part of my research is directed toward harnessing small mechanical devices for sensing applications. Nanoscale structures appear to offer revolutionary potential; the smaller a device, the more susceptible its physical properties to alteration. One example is resonant detectors, which are frequently used for sensing mass. The vibrations of a tiny mechanical element, such as a small cantilever, are intimately linked to the element's mass, so the addition of a minute amount of foreign material (the "sam-

The difficulties in communication between the nanoworld and the macroworld represent a central issue in the development of nanotechnology.

ple" being weighed) will shift the resonant frequency. Recent work in my lab by postdoc Kamil Ekinci shows that nanoscale devices can be made so sensitive that "weighing" individual atoms and molecules becomes feasible.

But there is a dark side. Gaseous atoms and molecules constantly adsorb and desorb from a device's surfaces. If the device is macroscopic, the resulting fractional change in its mass is negligible. But the change can be significant for nanoscale structures. Gases impinging on a resonant detector can change the resonant frequency randomly. Apparently, the smaller the device, the less stable it will be. This instability may pose a real disadvantage for various types of futuristic electromechanical signal-processing applications. Scientists might be able to work around the problem by, for example, using arrays of nanomechanical devices to average out fluctuations. But for individual elements, the problem seems inescapable.

A second example of how "not everything goes" in the nanoworld relates more to economics. It arises from the intrinsically ultralow power levels at which nanomechanical devices operate. Physics sets a fundamental threshold for the minimum operating power: the ubiquitous, random thermal vibrations of a mechanical device impose a "noise floor" below which real signals become increasingly hard to discern. In practical use, nanomechanical devices are optimally excited by signal levels 1,000-fold or a millionfold greater than this threshold. But such levels are still a millionth to a billionth the amount of power used for conventional transistors.

The advantage, in some future nanomechanical signal-processing system or computer, is that even a million nanomechanical elements would dissipate only a millionth of a watt, on average. Such ultralow power systems could lead to wide proliferation and distribution of

cheap, ultraminiature "smart" sensors that could continuously monitor *all* of the important functions in hospitals, in manufacturing plants, on aircraft, and so on. The idea of ultraminiature devices that drain their batteries extremely slowly, especially ones with sufficient computational power to function autonomously, has great appeal.

But here, too, there is a dark side. The regime of ultralow power is quite foreign to present-day electronics. Nanoscale devices will require entirely new system architectures that are compatible with amazingly low power thresholds. This prospect is not likely to be received happily by the computer industry, with its overwhelming investment in current devices and methodology. A new semiconductor processing plant today costs



RICHARD FEYNMAN predicted the rise of nanotechnology in a landmark 1959 talk at Caltech. "The principles of physics," he said, "do not speak against the possibility of maneuvering things atom by atom." But he also anticipated that unique laws would prevail; they are finally being discovered today.

more than \$1 billion, and it would probably have to be retooled to be useful. But I am certain that the revolutionary prospects of nanoscale devices will eventually compel such changes.

Monumental Challenges

CERTAINLY A HOST of looming issues will have to be addressed before we can realize the potential of nanoscale devices. Although each research area has its own concerns, some general themes emerge. Two challenges fundamental to my current work on nanomechanical systems, for instance, are relevant to nanotechnology in general.

Challenge 1: Communication between the macroworld and the nanoworld. NEMS are incredibly small, yet their motion can be far smaller. For example, a nanoscale beam clamped on both ends vibrates with minimal harmonic distortion when its vibration amplitude is kept below a small fraction of its thickness. For a 10-nanometer-thick beam, this amplitude is only a few nanometers. Building the requisite, highly efficient transducers to transfer information from such a device to the macroworld involves reading out information with even greater precision.

Compounding this problem, the natural frequency of the vibration increases as the size of the beam is decreased. So to usefully track the device's vibrations, the ideal NEMS transducer must be capable of resolving extremely small displacements, in the picometer-to-femtometer (trillionth to quadrillionth of a meter) range, across very large bandwidths (extending into the microwave range). These twin requirements pose a truly monumental challenge, one much more significant than those faced so far in MEMS work. A further complication is that most of the methodologies from MEMS are inapplicable; they simply do not scale down well to nanometer dimensions.

In each new regime, some wonderful scientific phenomenon emerges. But then a thorny host of underlying, equally unanticipated problems appear.

These difficulties in communication between the nanoworld and the macro-world represent a generic issue in the development of nanotechnology. Ultimately, the technology will depend on robust, well-engineered information transfer pathways from what are, in

essence, individual macromolecules. Although the grand vision of futurists may involve self-programmed nanobots that need direction from the macro-world only when they are first wound up and set in motion, it seems more likely that most nanotechnological applications re-

alizable in our lifetimes will entail some form of reporting up to the macro-world and feedback and control back down. The communication problem will remain central.

Orchestrating such communication immediately invokes the very real possibility of collateral damage. Quantum theory tells us that the process of measuring a quantum system nearly always perturbs it. This can hold true even when we scale up from atoms and molecules to nanosystems comprising millions or billions of atoms. Coupling a nanosystem to probes that report back to the macro-world always changes the nanosystem's properties to some degree, rendering it less than ideal. Introducing the transducers required for communication will do more than just increase the nanosystem's size and complexity. They will also necessarily extract some energy to perform their measurements and can degrade the nanosystem's performance. Measurement always has its price.

Challenge II: Surfaces. As we shrink MEMS to NEMS, device physics becomes increasingly dominated by the surfaces. Much of the foundation of solid-state physics rests on the premise that the surface-to-volume ratio of objects is infinitesimal, meaning that physical properties are always dominated by the physics of the bulk. Nanoscale systems are so small that this assumption breaks down completely.

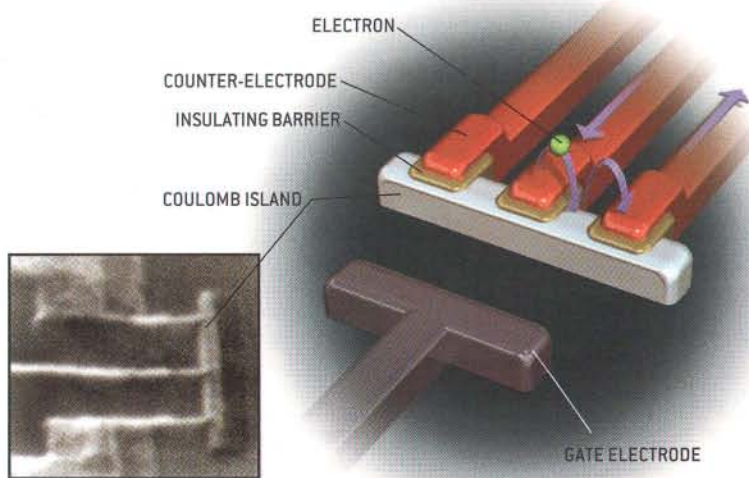
For example, mechanical devices patterned from single-crystal, ultrapure materials can contain very few (even zero) crystallographic defects and impurities. My initial hope was that, as a result, there would be only very weak damping of mechanical vibrations in monocrystalline NEMS. But as we shrink mechanical devices, we repeatedly find that acoustic energy loss seems to increase in proportion to the increasing surface-to-

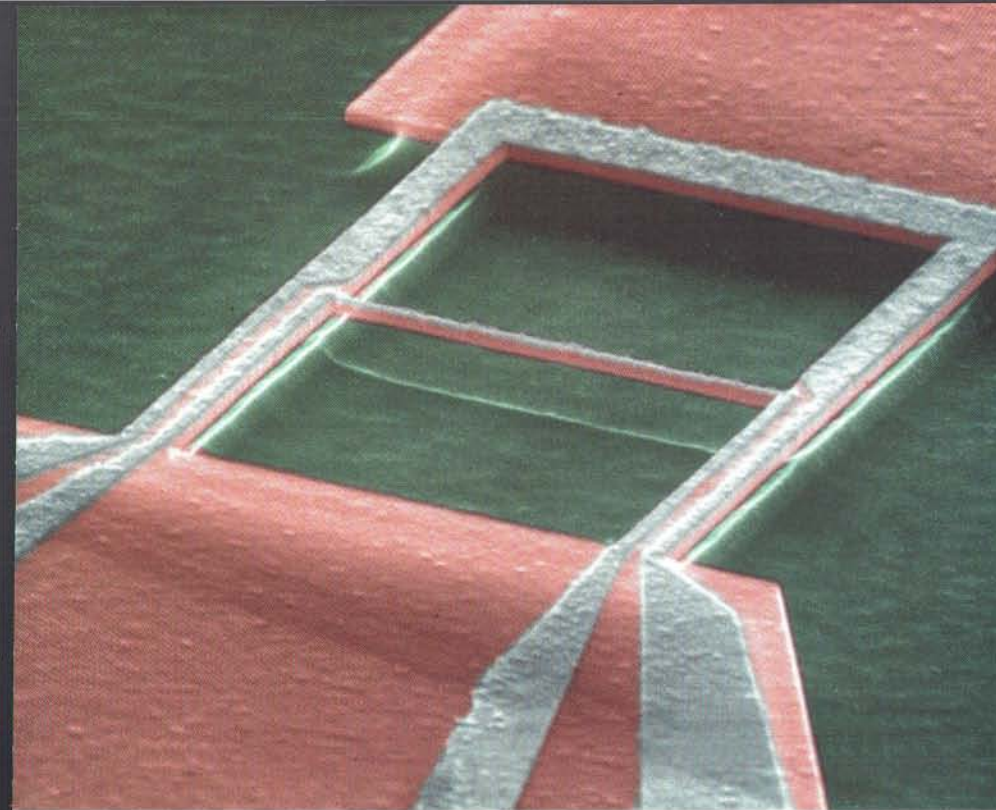
TAKING CHARGE

SINGLE ELECTRONICS

Advances in nanofabrication allowed Theodore A. Fulton and Gerald J. Dolan to build a single-electron transistor at Bell Laboratories in 1987 (*micrograph*). In this structure the controlled movement of individual electrons through a nanodevice was first achieved. At its heart was a coulomb island, a metallic electrode isolated from its counter-electrodes by thin insulating oxide barriers (*diagram*). The counter-electrodes led up to the macroscale laboratory instrumentation used to carry out the experiments. An additional gate electrode (visible in the diagram but not the micrograph) was offset from the coulomb island by a small gap; it allowed direct control of the charge introduced to the island. Electric current flowed through the device from one counter-electrode to another, as in a conventional circuit, but here it was limited by the stepwise hopping of electrons onto and off the coulomb island.

Fulton and Dolan's experiments demonstrate both the fundamental physics of single-electron charging and the potential of these devices as ultrasensitive electrometers: instruments that can easily detect individual electron charges. Circuits that switch one electron at a time could someday form the basis for an entirely new class of nanoelectronics. The advent of such single electronics, however, also presages problems that will have to be faced as conventional electronic circuits are shrunk to the nanoscale.





NANOMECHANICAL AMPLIFIER overcomes the vexing problem of communication with the macroworld by providing up to 1,000-fold amplification of weak forces. Two suspended bridges (*left and right*) of monocrystalline silicon carbide support the central crossbridge, to which the signal force is applied. Thin-film electrodes (*silver*) atop these structures provide very sensitive readouts of nanoscale motion.

volume ratio. This result clearly implicates surfaces in the devices' vibrational energy-loss processes. In a state-of-the-art silicon beam measuring 10 nanometers wide and 100 nanometers long, more than 10 percent of the atoms are at or next to the surface. It is evident that these atoms will play a central role, but understanding precisely *how* will require a major, sustained effort.

In this context, so-called nanotube structures, which have been heralded lately, look ideal. A nanotube is a crystalline, rodlike material perfect for building the miniature vibrating structures of interest to us. And because it has no chemical groups projecting outward along its length, one might expect that interaction with "foreign" materials at its surfaces would be minimal. Apparently not. Although nanotubes exhibit ideal characteristics when shrouded within pristine, ultrahigh vacuum environments, samples in more ordinary conditions, where they are exposed to air or water vapor, evince electronic properties that are markedly different. Mechanical properties are likely to show similar sensitivity. So surfaces definitely *do* matter. It would seem there is no panacea.

Payoff in the Glitches

FUTURISTIC THINKING is crucial to making the big leaps. It gives us some wild and crazy goals—a holy grail to chase. And the hope of glory propels us onward. Yet the famous 19th-century chemist Kekulé once said, "Let us learn to dream, gentlemen, then perhaps we shall find the truth.... But let us beware of publishing our dreams before they have been put to the proof by the waking understanding."

This certainly holds for nanoscience. While we keep our futuristic dreams alive, we also need to keep our expectations realistic. It seems that every time we gain access to a regime that is a factor of 10 different—and presumably "better"—two things happen. First, some wonderful, unanticipated scientific phenomenon emerges. But then a thorny host of underlying, equally unanticipated new problems appear. This pattern has held

true as we have pushed to decreased size, enhanced sensitivity, greater spatial resolution, higher magnetic and electric fields, lower pressure and temperature, and so on. It is at the heart of why projecting forward too many orders of magnitude is usually perilous. And it is what should imbue us with a sense of humility and proportion at this, the beginning of our journey. Nature has already set the rules for us. We are out to understand and employ her secrets.

Once we head out on the quest, nature will frequently hand us what initially seems to be nonsensical, disappointing, random gibberish. But the science in the glitches often turns out to be even more important than the grail motivating the quest. And being proved the fool in this way can truly be the joy of doing science. If we had the power to extrapolate everything correctly from the outset, the pursuit of science would be utterly dry and mechanistic. The delightful truth is that, for complex systems, we do not, and ultimately probably cannot, know everything that is important.

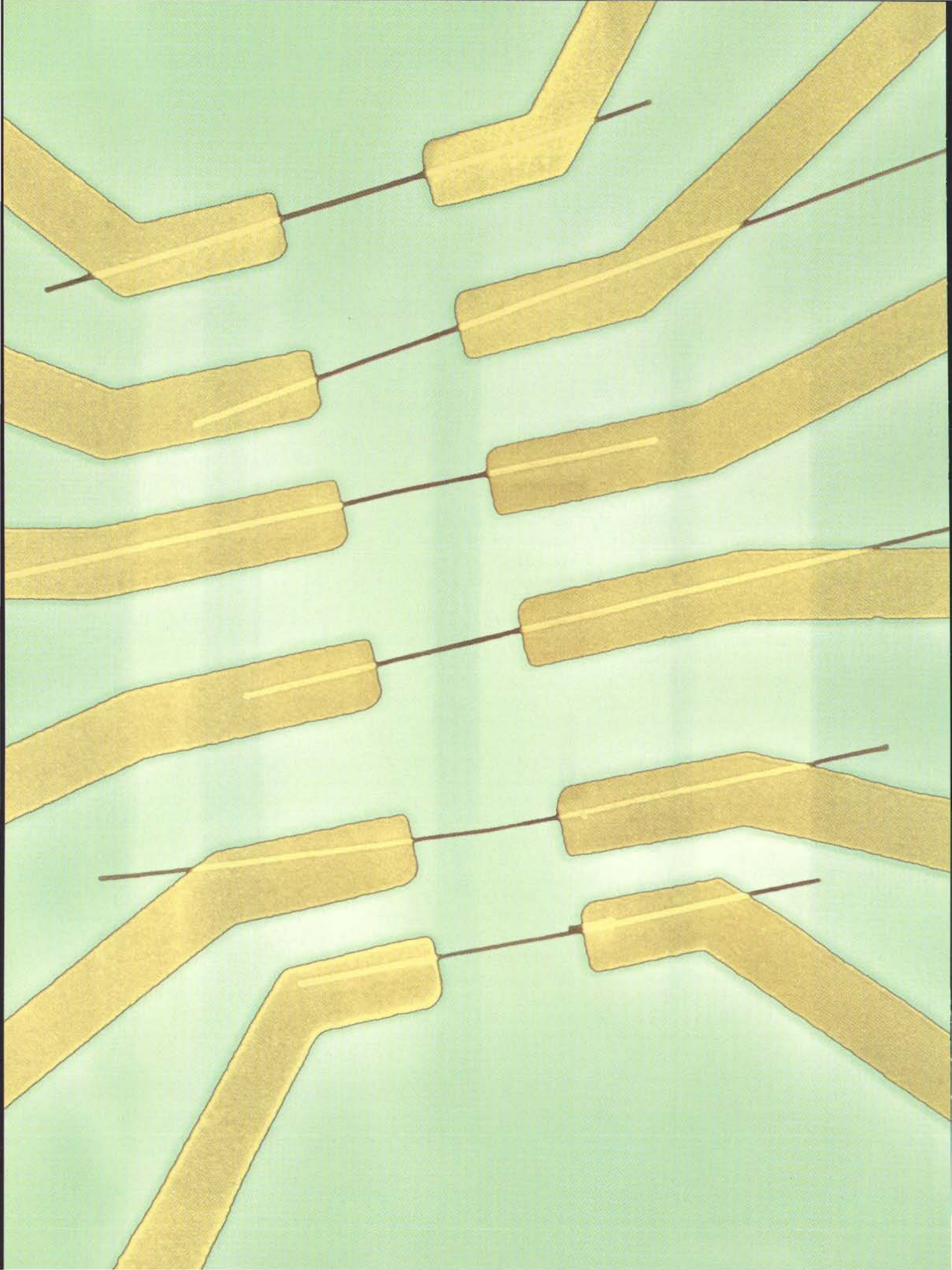
Complex systems are often exquisitely sensitive to a myriad of parameters beyond our ability to sense and record—much less control—with sufficient regularity and precision. Scientists have studied, and in large part already understand, matter down to the fundamental particles that make up the neutrons, protons and electrons that are of crucial importance to chemists, physicists and engineers. But we still cannot deterministically predict how arbitrarily complex assemblages of these three elemental components will finally behave en masse. For this reason, I firmly believe that it is on the foundation of the experimental science already under way, in intimate collaboration with theory, that we will build the road to true nanotechnology. Let's keep our eyes open for surprises along the way!

MORE TO EXPLORE

Nanoelectromechanical Systems Face the Future. Michael Roukes in *Physics World*, Vol. 14, No. 2; February 2001. Available at physicsweb.org/article/world/14/2/8

The author's group: www.its.caltech.edu/~nano

Richard Feynman's original lecture "There's Plenty of Room at the Bottom" can be read at www.its.caltech.edu/~feynman



The Incredible Shrinking Circuit

RESEARCHERS HAVE BUILT
NANOTRANSISTORS AND NANOWIRES.
NOW THEY JUST NEED TO FIND A WAY
TO PUT THEM ALL TOGETHER

BY CHARLES M. LIEBER

NANOWIRES, each about five to 10 nanometers in diameter, may represent the future of electronics. They are the brown lines, made of indium phosphide, connecting the gold electrodes in this micrograph. These wires have been put to truly diverse uses—as memory and logic and as arrays of light-emitting diodes.

Do we really need to keep on making circuits smaller? The miniaturization of silicon microelectronics seems so inexorable that the question seldom comes up—except maybe when we buy a new computer, only to find that it becomes obsolete by the time we leave the store. A state-of-the-art microprocessor today has more than 40 million transistors; by 2015 it could have nearly five billion. Yet within the next two decades this dramatic march forward will run up against scientific, technical and economic limits. A first reaction might be, So what? Aren't five billion transistors enough already?

Yet when actually confronted with those limits, people will no doubt want to go beyond them. Those of us who work to keep computer power growing are motivated in part by the sheer challenge of discovering and conquering unknown territory. But we also see the potential for a revolution in medi-

els of organization. The basic building block is usually the transistor or its nanoequivalent—a switch that can turn an electric current on or off as well as amplify signals. In microelectronics, transistors are made out of chunks of semiconductor—a material, such as impure silicon, that can be manipulated to flip between conducting and nonconducting states. In nanoelectronics, transistors might be organic molecules or nanoscale inorganic structures.

The next level of organization is the interconnection—the wires that link transistors together in order to perform arithmetic or logical operations. In microelectronics, wires are metal lines typically hundreds of nanometers to tens of microns in width deposited onto the silicon; in nanoelectronics, they are nanotubes or other wires as narrow as one nanometer.

At the top level is what engineers call architecture—the over-

The use of molecules for electronic devices remained theoretical until a recent confluence of advances in chemistry, physics and engineering.

cine and so many other fields, as extreme miniaturization enables people and machines to interact in ways that are not possible with existing technology.

As the word suggests, microelectronics involves components that measure roughly one micron on a side (although lately the components have shrunk to a size of almost 100 nanometers). Going beyond microelectronics means more than simply shrinking components by a factor of 10 to 1,000. It also involves a paradigm shift for how we think about putting everything together.

Microelectronics and nanoelectronics both entail three lev-

els of organization. The basic building block is usually the transistor or its nanoequivalent—a switch that can turn an electric current on or off as well as amplify signals. In microelectronics, transistors are made out of chunks of semiconductor—a material, such as impure silicon, that can be manipulated to flip between conducting and nonconducting states. In nanoelectronics, transistors might be organic molecules or nanoscale inorganic structures.

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Overview/*Nanoelectronics*

- Silicon chips, circuit boards, soldering irons: these are the icons of modern electronics. But the electronics of the future may look more like a chemistry set. Conventional techniques can shrink circuits only so far; engineers will soon need to shift to a whole new way of organizing and assembling electronics. One day your computer may be built in a beaker.
- Researchers have created nanometer-scale electronic components—transistors, diodes, relays, logic gates—from organic molecules, carbon nanotubes and semiconductor nanowires. Now the challenge is to wire these tiny components together.
- Unlike conventional circuit design, which proceeds from blueprint to photographic pattern to chip, nanocircuit design will probably begin with the chip—a haphazard jumble of as many as 10^{24} components and wires, not all of which will even work—and gradually sculpt it into a useful device.

Smallifying Machines

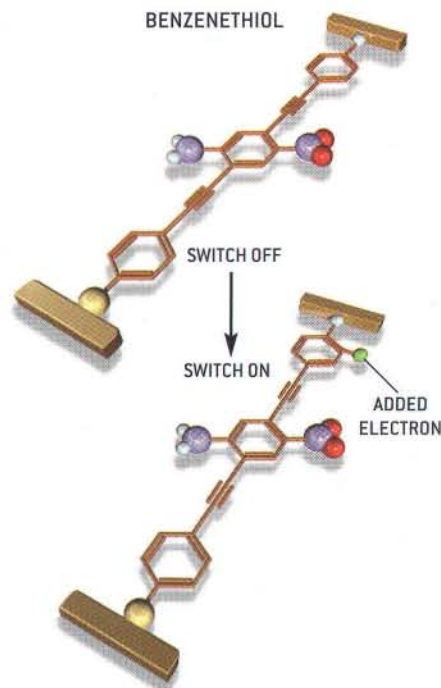
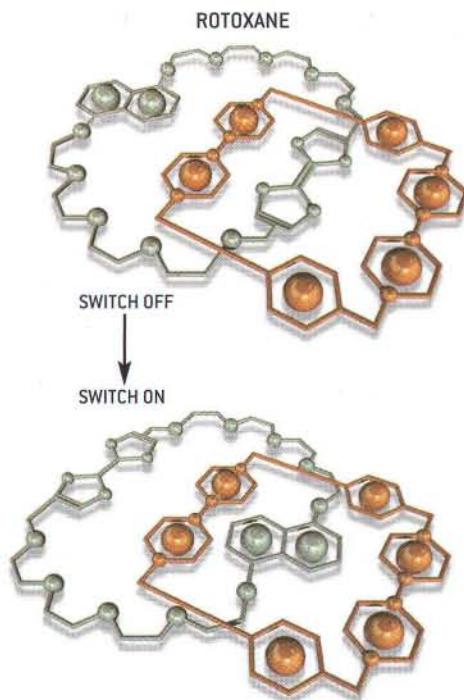
THE USE OF MOLECULES for electronic devices was suggested more than a quarter of a century ago in a seminal paper by Avi Aviram of IBM and Mark A. Ratner of Northwestern University. By tailoring the atomic structures of organic molecules, they proposed, it should be possible to concoct a transistorlike device. But their ideas remained largely theoretical until a recent confluence of advances in chemistry, physics and engineering.

Of all the groups that have turned Aviram and Ratner's

NANOTRANSISTORS

MOLECULAR TRANSISTORS

could be the building blocks of electronics on the nanometer scale. Each of the two molecules shown here conducts electricity like a tiny wire once a chemical reaction—oxidation reduction—alters its atomic configuration and switches it on. In the diagram, each stick represents a chemical bond; each intersection of two sticks represents a carbon atom; and each ball represents an atom other than carbon.



ideas into reality, two teams—one at the University of California at Los Angeles and Hewlett-Packard, the other at Yale, Rice and Pennsylvania State universities—stand out. Within the past year, both have demonstrated that thousands of molecules clustered together can carry electrons from one metal electrode to another. Each molecule is about 0.5 nanometer wide and one or more nanometers long. Both groups have shown that the clusters can behave as on/off switches and might thus be usable in computer memory; once on, they will stay on for 10 minutes or so [see “Computing with Molecules,” by Mark A. Reed and James M. Tour; *SCIENTIFIC AMERICAN*, June 2000]. That may not sound like a long time, but computer memory typically loses its information instantly when the power is turned off; even when the power is on, the stored information leaks away and must be “refreshed” every 0.1 second or so.

Although the details differ, the switching mechanism for both molecules is believed to involve a well-understood chemical reaction, oxidation reduction, in which electrons shuffle among atoms within the molecule. The reaction puts a twist in the molecule, blocking electrons as surely as a kink in a hose blocks water [see illustration above]. In the “on” position, the clusters of molecules may conduct electricity as much as 1,000 times better than in the “off” position. That ratio is actually rather low compared with that of typical semiconductor transistors, whose conductivity varies a millionfold. Researchers are now looking for other molecules with even better switching properties and are also working to understand the switching process itself.

My own research group at Harvard University is one of several that have focused not on organic molecules but on long, thin inorganic wires. The best-known example is the carbon nanotube, which is typically about 1.4 nanometers in diameter [see “Nanotubes for Electronics,” by Philip G. Collins and Phaedon Avouris; *SCIENTIFIC AMERICAN*, December 2000]. Not only can these nanoscale wires carry much more current, atom for atom, than ordinary metal wires, they can also act as tiny transistors. By functioning both as interconnections and as components, nanowires kill two birds with one stone. Another advantage is that they can exploit the same basic physics as standard silicon microelectronics, which makes them easier to understand and manipulate.

In 1997 Cees Dekker’s group at the Delft University of Technology in the Netherlands and Paul L. McEuen’s group, then at the University of California at Berkeley, independently reported highly sensitive transistors made from metallic carbon nanotubes. These devices could be turned on and off by a

THE AUTHOR

CHARLES M. LIEBER spent much of his childhood building—and breaking—stereos, cars and model airplanes. He is now the Mark Hyman Professor of Chemistry at Harvard University, where he directs a group of 25 undergraduate, graduate and postdoctoral researchers who focus on nanoscale science and technology. Lieber recently founded NanoSys, Inc., with Larry Bock of CW Ventures and Hongkun Park of Harvard. Their modest goal: to revolutionize chemical and biological sensing, electronics, optoelectronics, and information storage.

single electron but required very low temperatures to operate. This past July Dekker's team swept away this limitation. The researchers used an atomic force microscope to create a single-electron transistor that could function at room temperature. Dekker and his co-workers have also fashioned a more conventional field-effect transistor, the building block of most integrated circuits today, out of a carbon nanotube, and McEuen's group has combined metallic and semiconductor nanotubes into

a diode, which allows electric current to pass in one direction only. Finally, my group has demonstrated a very different type of switch, a nanoscale electromechanical relay.

Hot Wire

A MAJOR PROBLEM with nanotubes is that they are difficult to make uniform. Because a slight variation in diameter can spell the difference between a conductor and a semiconductor,

DNA Computing

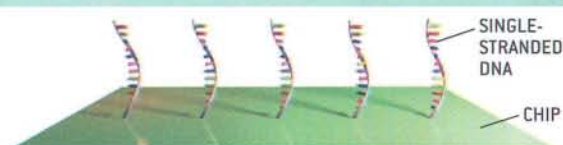
WHY LIMIT OURSELVES TO ELECTRONICS? Most efforts to shrink computers assume that these machines will continue to operate much as they do today, using electrons to carry information and transistors to process it. Yet a nanoscale computer could operate by completely different means. One of the most exciting possibilities is to exploit the carrier of genetic information in living organisms, DNA.

The molecule of life can store vast quantities of data in its sequence of four bases (adenine, thymine, guanine and cytosine), and natural enzymes can manipulate this information in a highly parallel manner. The power of this approach was first brought to light by computer scientist Leonard M. Adleman in 1994. He showed that a DNA-based computer could solve a type of problem that is particularly difficult for ordinary computers—the Hamiltonian path problem, which is related to the infamous traveling-salesman problem [see "Computing with DNA," by Leonard M. Adleman; *SCIENTIFIC AMERICAN*, August 1998].

Adleman started by creating a chemical solution of DNA. The individual DNA molecules encoded every possible pathway between two points. By going through a series of separation and amplification steps, Adleman weeded out the wrong paths—those, for example, that contained points they were not supposed to contain—until he had isolated the right one. More recently, Lloyd M. Smith's group at the University of Wisconsin–Madison implemented a similar algorithm using gene chips, which may lend themselves better to practical computing (*diagram*).

Despite the advantages of DNA computing for otherwise intractable problems, many challenges remain, including the high incidence of errors caused by base-pair mismatches and the huge number of DNA nanoelements needed for even a modest computation. DNA computing may ultimately merge with other types of nanoelectronics, taking advantage of the integration and sensing made possible by nanowires and nanotubes.

—C.M.L.



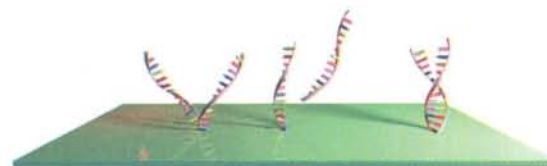
1 Single DNA strands are attached to a silicon chip. They encode all possible values of the variables in an equation that the researchers want to solve.



2 Copies of a complementary strand—which encodes the first clause of the equation—are poured onto the chip. These copies attach themselves to any strand that represents a valid solution of the clause. Any invalid solutions remain a single strand.



3 An enzyme removes all the single strands.



4 Other processes melt away the added complementary strands. These steps are repeated with all the clauses of the equation.



5 The DNA strand that survives this whole process represents the solution to the whole equation.

Soon nanodevices may have useful applications—for example, as ultrasensitive detectors of gas molecules and biological compounds.

a large batch of nanotubes may contain only a few working devices. In April of this year Phaedon Avouris and his colleagues at the IBM Thomas J. Watson Research Center came up with a solution. They started with a mixture of conducting and semiconducting nanotubes and, by applying a current between metal electrodes, selectively burned away the conducting ones until just semiconducting ones were left. The solution is only partial, however, because it requires the use of conventional lithography to wire up the random nanotube array and then test and modify each of the individual elements, which would ultimately number in the billions.

My group has also been working on a different type of nanoscale wire, which we term the semiconductor nanowire. It is about the same size as a carbon nanotube, but its composition is easier to control precisely. To synthesize these wires, we start with a metal catalyst, which defines the diameter of the growing wire and serves as the site where molecules of the desired material tend to collect. As the nanowires grow, we incorporate chemical dopants (impurities that add or remove electrons), thereby controlling whether the nanowires are *n*-type (having extra electrons) or *p*-type (having a shortage of electrons or, equivalently, a surfeit of positively charged “holes”).

The availability of *n*- and *p*-type materials, which are the essential ingredients of transistors, diodes and other electronic devices, has opened up a new world for us. We have assembled a wide range of devices, including both major types of transistors (field-effect and bipolar); inverters, which transform a “0” signal to a “1”; and light-emitting diodes, which pave the way for optical interconnections. Our bipolar transistors were the first molecular-scale devices ever to amplify a current. A recent advance in my lab by Xiangfeng Duan has been the assembly of memory from crisscrossing *n*- and *p*-type nanowires. The memory can store information for 10 minutes or longer by trapping charge at the interface between the crossing nanowires [see illustration on next page].

Breaking the Logjam

BUILDING UP AN ARSENAL of molecular and nanoscale devices is just the first step. Interconnecting and integrating these devices is perhaps the much greater challenge. First, the nanodevices must be connected to molecular-scale wires. To date, organic-molecule devices have been hooked up to conventional metal wires created by lithography. It will not be easy to substitute nanowires, because we do not know how to make a good electrical connection without ruining these tiny wires in the process. Using nanowires and nanotubes both for the devices and for the interconnections would solve that problem.

Second, once the components are attached to nanowires, the

wires themselves must be organized into, for example, a two-dimensional array. In a report published earlier this year, Duan and another member of my team, Yu Huang, made a very significant breakthrough: they assembled nanocircuits by means of fluid flows. Just as sticks and logs can flow down a river, nanoscale wires can be drawn into parallel lines using fluids. In my lab we have used ethanol and other solutions and controlled the liquid flow by passing it through channels molded into polymer blocks, which can be easily placed on the substrate where we wish to assemble devices.

The process creates interconnections in the direction of the fluid flow: if the flow is along only one channel, then parallel nanowires are formed. To add wires in other directions, we redirect the flow and repeat the process, building up additional layers of nanowires. For instance, to produce a right-angle grid, we first lay down a series of parallel nanowires, then rotate the direction of flow by 90 degrees and lay down another series. By using wires of different compositions for each layer, we can rapidly assemble an array of functional nanodevices using equipment not much more sophisticated than a high school chemistry lab. A grid of diodes, for example, consists of a layer of conducting nanotubes above a layer of semiconductor nanotubes, or a layer of *n*-type nanowires atop a layer of *p*-type nanowires. In both cases, each junction serves as a diode.

Our approach, which is similar to that being pursued by the team at U.C.L.A. and Hewlett-Packard, is deterministic. We are trying to create arrays with a certain predictable behavior. Form follows function. An alternative proposed by the group at Rice, Yale and Penn State is to allow blocks of devices and wires to interconnect at random. Later, the ensemble can be analyzed to determine how it might be used for storage or computation. In this case, function follows form. The problem with this procedure is that it would take a huge effort to map a complex network and figure out what use it could be put to.

Intimately linked to all these efforts is the development of architectures that best exploit the unique features of nanoscale devices and the capabilities of bottom-up assembly. Although we can make unfathomable numbers of dirt-cheap nanostructures, the devices are much less reliable than their microelectronic counterparts, and our capacity for assembly and organization is still quite primitive.

In collaboration with André DeHon of the California Institute of Technology, my group has been working on highly simplified architectures that can be generalized for universal computing machines. For memory, the architecture starts with a two-dimensional array of crossed nanowires or suspended electromechanical switches in which one can store information at each cross point. The same basic architecture is being pur-

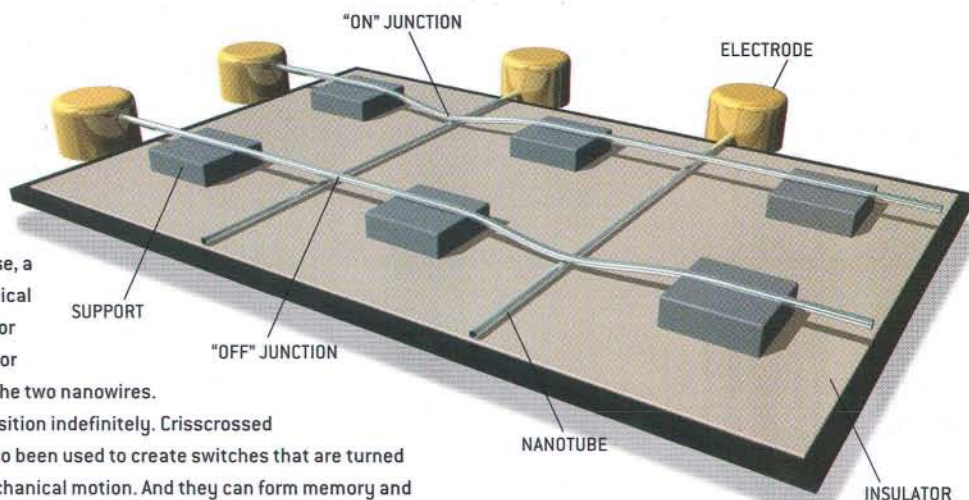
NANOWIRE ARRAY

CRISSCROSSING NANOWIRES

neatly solves a major problem in molecular-scale electronics:

How do you connect wires to components such as transistors or diodes? The wires do double duty, serving both as wires and as components. Each junction is a component, in this case, a miniature relay—an electromechanical switch that is either on (*touching*) or off (*separated*). To flip a switch on or off, you apply a certain voltage to the two nanowires.

The switch will then stay in that position indefinitely. Crisscrossed semiconductor nanowires have also been used to create switches that are turned on and off electrically, without mechanical motion. And they can form memory and logic arrays—key steps toward the assembly of a nanocomputer.



sued by researchers at U.C.L.A. and Hewlett-Packard, and it resembles the magnetic-core memory that was common in computers of the 1950s and 1960s.

Law of Large Numbers

TO OVERCOME the unreliability of individual nanodevices, we may rely on sheer numbers—the gizmos are so cheap that plenty of spares are always available. Researchers who work on defect tolerance have shown that computing is possible even if many of the components fail, although identifying and mapping the defects can be slow and time-consuming. Ultimately we hope to partition the enormous arrays into subarrays whose reliability can be easily monitored. The optimum size of these subarrays will depend on the defect levels typically present in molecular and nanoscale devices.

Another significant hurdle faced by nanoelectronics is “bootstrapping.” How do engineers get the circuit to do what they want it to? In microelectronics, circuit designers work like architects: they prepare a blueprint of a circuit, and a fabrication plant builds it. In nanoelectronics, designers will have to work like computer programmers. A fabrication plant will create a raw nanocircuit—billions on billions of devices and wires whose functioning is rather limited. From the outside, it will look like a lump of material with a handful of wires sticking out. Using those few wires, engineers will somehow have to configure those billions of devices. Challenges such as this are what keeps me tremendously excited about the field as a whole.

Even before we solve these problems, nanodevices may have useful applications. For example, semiconducting carbon nanotubes have been used by Hongjie Dai’s group at Stanford University to detect gas molecules, and Yi Cui in my group has used semiconductor nanowires as ultrasensitive detectors for a wide

range of biological compounds. In our work at Harvard, we have converted nanowire field-effect transistors into sensors by modifying their surfaces with molecular receptors. This technology has the potential of detecting single molecules using only a voltmeter from a hardware store. The small size and sensitivity of nanowires also make possible the assembly of extremely powerful sensors that could, for instance, sequence the entire human genome on a single chip and serve in minimally invasive medical devices. In the nearer term, we could see hybrids of micro and nano: silicon with a nano core—perhaps a high-density computer memory that retains its contents forever.

Although substantial work remains before nanoelectronics makes its way into computers, this goal now seems less hazy than it was even a year ago. As we gain confidence, we will learn not just to shrink digital microelectronics but also to go where no digital circuit has gone before. Nanoscale devices that exhibit quantum phenomena, for example, could be exploited in quantum encryption and quantum computing. The richness of the nanoworld will change the macroworld. SD

MORE TO EXPLORE

The author’s Web site: cmlliris.harvard.edu

The Avouris group: www.research.ibm.com/nanoscience

The Dai group: www-chem.stanford.edu/group/dai

The DeHon group: www.cs.caltech.edu/~andre

The Dekker group: www.mb.tn.tudelft.nl/user/dekker

The McEuen group:

www.lassp.cornell.edu/lassp_data/mceuen/homepage/welcome.html

The Penn State team: stm1.chem.psu.edu

The Rice/Yale team: www.jmtour.com and www.eng.yale.edu/reedlab

The Smith group: www.chem.wisc.edu/~smith

The U.C.L.A./Hewlett-Packard team: www.chem.ucla.edu/~schung/hgrp and www.hpl.hp.com/research/qsr/staff/kuekes.html

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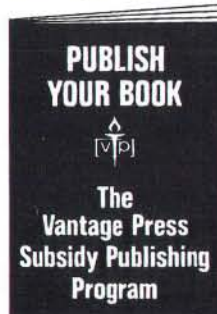
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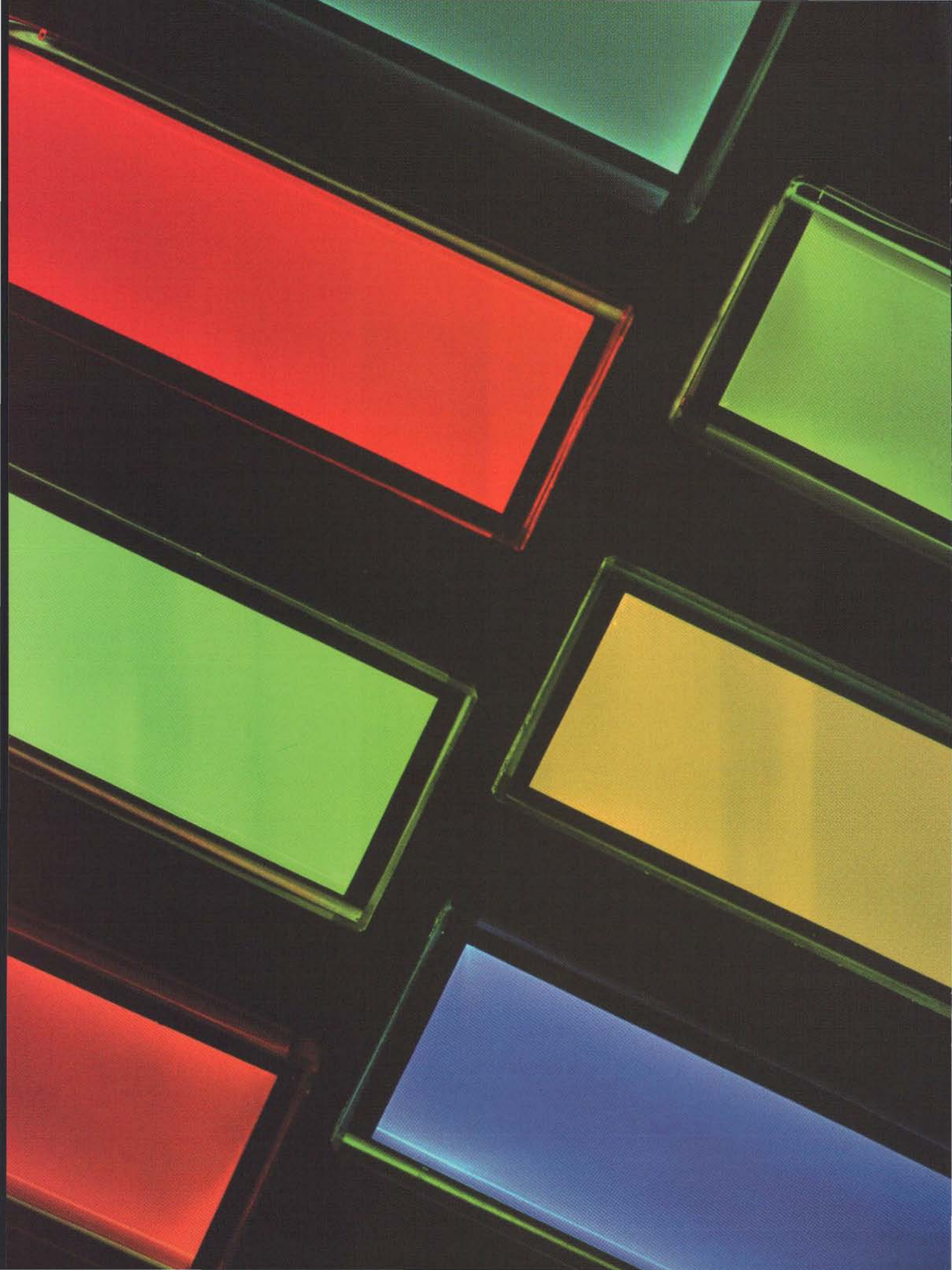
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Less **is** more in Medicine

BY A. PAUL ALIVISATOS

The 1966 film *Fantastic Voyage* treated moviegoers to a bold vision of nanotechnology applied to medicine: through mysterious means, an intrepid team of doctors and their high-tech submarine were shrunk to minute size so that they could travel through the bloodstream of an injured patient and remove a life-threatening blood clot in his brain. In the past 35 years, great strides have been made in fabricating complex devices at ever smaller scales, leading some people to believe that such forms of medical intervention are possible and that tiny robots will soon be coursing through everyone's veins. Indeed, in some circles the idea is taken so seriously that worries have emerged about the dark side of such technology: Could

HIGHLY MAGNIFIED VIALS contain solutions of quantum dots—semiconductor nanocrystals—of specific sizes. The precise size of a quantum dot determines the color it emits after exposure to light. By attaching different sizes of dots to different biological molecules, investigators can track the activities of many tagged molecules simultaneously.

SOPHISTICATED FORMS OF NANOTECHNOLOGY WILL FIND SOME OF THEIR FIRST REAL-WORLD APPLICATIONS IN BIOMEDICAL RESEARCH, DISEASE DIAGNOSIS AND, POSSIBLY, THERAPY

self-replicating nanometer-scale automatons run amok and destroy the entire biological world?

In my view, shared by most investigators, such thoughts belong squarely in the realm of science fiction. Still, nanotechnology can potentially enhance biomedical research tools—for example, by providing new kinds of labels for experiments done to discover drugs or to reveal which sets of genes are active in cells under various conditions. Nanoscale devices could, moreover, play a part in quick diagnostic screens and in genetic tests, such as those meant to determine a person's susceptibility to different disorders or to reveal which specific genes are mutated in a patient's cancer. Investigators are also studying them as improved contrast agents for noninvasive imaging and as drug-delivery vehicles. The emerging technologies may not be as photogenic as a platelet-size Raquel Welch blasting away at a clot with a laser beam, but they are every bit as dramatic because, in contrast, the benefits they offer to patients and researchers are real.

The technologies may not be as photogenic as a minute Raquel Welch blasting away at a clot, but they are just as dramatic because their benefits are real.

How exactly can nanotechnology do all these things? The answer hinges on one's definitions. All of biology is arguably a form of nanotechnology. After all, even the most complicated creature is made up of tiny cells, which themselves are constructed of nanoscale building blocks: proteins, lipids, nucleic acids and other complex biological molecules. But by convention the term "nanotechnology" is usually restricted to artificial constructions made, say, from semiconductors, metals, plastic or glass. A few inorganic structures of nanometer scale—minute crystals, for instance—have already been commercialized, notably as contrast agents.

Magnetic Attraction

NATURE ITSELF provides a beautiful illustration of the usefulness of such inorganic crystals in a biological context: humble magnetotactic (magnetic-sensing) bacteria. Such organisms, which live in bodies of water and their muddy bottoms, thrive only at one depth in the water or sediment. Above this position, oxygen is too abundant for their liking; below, too scarce. A bacterium that drifts away from the right level must swim back, and so, like many of its cousins, the microbe wields a whiplike tail for propulsion. But how does the buoyant cell tell up from down when gravity has essentially no effect on it?

The answer is that this bacterium has fixed within it a chain of about 20 magnetic crystals that are each between 35 and 120 nanometers in diameter. Together these crystals constitute a miniature compass. Because the magnetic field of the earth is inclined in most places (it points not only north but also downward in the Northern Hemisphere and upward in the Southern), a magnetotactic bacterium can follow a magnetic field line up or down to its desired destination.

This compass is a marvel of natural nanoscale engineering. For one, it is made of the perfect material—either magnetite or greigite, both highly magnetic iron minerals. The use of multiple crystals is also no accident. At very small scales, the larger a magnetic particle is, the longer it stays magnetized. But if the particle becomes too large, it will spontaneously form two separate magnetic domains with oppositely directed magnetizations. Such a crystal has little overall magnetization and does not make for a very effective compass needle. By building its compass out of crystals that are of just the right size to exist as stable, single magnetic domains, the bacterium makes the best use of every bit of iron it lays down. Interestingly, when people design media for hard-disk storage, they follow exactly the same strategy, using magnetic nanocrystals that are of the proper size to be both stable and strong.

Artificial magnetic crystals of similar dimension might soon serve biomedical research in a novel way. Two groups, one in Germany and the other at my institution, the University of California at Berkeley, are exploring the use of magnetic nanoparticles to detect particular biological entities, such as microorganisms that cause disease.

Their method, like many of the techniques applied today, requires suitable antibodies, which bind to specific targets. The magnetic particles are affixed, as labels, to selected antibody molecules, which are then applied to the sample under study. To detect whether the antibodies have latched onto their target, an investigator applies a strong magnetic field (which temporarily magnetizes the particles) and then examines the specimen with a sensitive instrument capable of detecting the weak magnetic fields emanating from the probes. Labeled antibodies that have not docked to the sample tumble about so rapidly in solution that they give off no magnetic signal. Bound antibodies, however, are unable to rotate, and together their magnetic tags generate a readily detectable magnetic field.

Because the unbound probes produce no signal, this approach does away with the time-consuming washing steps usually required of such assays. The sensitivity demonstrated with this experimental technique is already better than with standard methods, and anticipated improvements in the apparatus should soon boost sensitivity by a factor of several hundred.

Despite these advantages, the magnetic method probably will not completely replace the widespread practice of labeling probes with a fluorescent tag, typically an organic molecule that glows with a characteristic hue when it is energized by light of a particular color. Colors are very useful in various diagnostic and research procedures, such as when more than one probe needs to be tracked.

Overview/*Nanomedicine*

- Nanometer-scale objects made of inorganic materials can serve in biomedical research, disease diagnosis and even therapy.
- Biological tests measuring the presence or activity of selected substances become quicker, more sensitive and more flexible when certain nanoscale particles are put to work as tags, or labels.
- Nanoparticles could be used to deliver drugs just where they are needed, avoiding the harmful side effects that so often result from potent medicines.
- Artificial nanoscale building blocks may one day be used to help repair such tissues as skin, cartilage and bone—and they may even help patients to regenerate organs.

A GRAND PLAN FOR MEDICINE

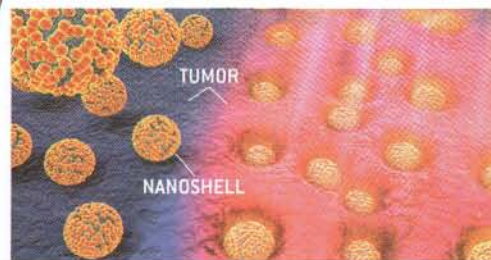
The National Nanotechnology Initiative includes among its goals, or "grand challenges," a host of futuristic improvements in the detection, diagnosis and treatment of disease. Some are depicted here. The goals, many of which are far from being realized, also feature new aids for vision and hearing, rapid tests for detecting disease susceptibility and responses to drugs, and tiny devices able to find problems—such as incipient tumors, infections or heart problems—and to relay the information to an external receiver or fix them on the spot.

1 GOAL: Improved Imaging

Improved or new contrast agents would detect problems at earlier, more treatable stages. They might, for instance, reveal tumors (red) only a few cells in size.

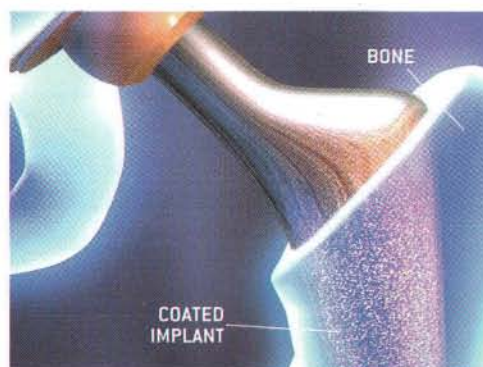


2 GOAL: New Ways to Treat Disease



Nanoparticles would deliver treatments to specifically targeted sites, including places that standard drugs do not reach easily. For example, gold nanoshells (spheres) that were targeted to tumors might, when hit by infrared light, heat up enough to destroy the growths.

3 GOAL: Superior Implants



Nanometer-scale modifications of implant surfaces would improve implant durability and biocompatibility. For instance, an artificial hip coated with nanoparticles might bond to the surrounding bone more tightly than usual, thus avoiding loosening.

The world of modern electronics is also full of light-emitting materials. Every CD player, for instance, reads the disc with light from a solid-state laser diode, which is made of an inorganic semiconductor. Imagine carving out a vanishingly small piece of that material, a scoop the size of a protein molecule. The result is a semiconductor nanocrystal, or, in the talk of the trade, a "quantum dot." Like nanoscale magnetic crystals, these minuscule dots have much to offer biomedical researchers.

As the name suggests, quantum dots owe their special properties to the weird rules of quantum mechanics, the same

rules that restrict the electrons in atoms to certain discrete energy levels. An organic dye molecule absorbs only photons of light with just the right energy to lift its electrons from their quiescent state to one of the higher levels available to them. That is, the incident light must be exactly the right wavelength, or color, to do the job. The molecule will subsequently

emit a photon when the electron falls back to a lower energy level. This phenomenon is quite different from what happens in bulk semiconductors, which allow electrons to occupy two broad bands of energy. Such materials can absorb photons in a broad range of colors (all those that have enough energy to bridge the gap between these two bands),

THE AUTHOR

A. PAUL ALIVISATOS is a professor in the department of chemistry at the University of California, Berkeley, where he received his doctorate in physical chemistry in 1986. A Fellow of both the American Association for the Advancement of Science and the American Physical Society, Alivisatos has received many awards for his research on the physical properties of nanocrystals. He is a founder of Quantum Dot Corporation, which is working to commercialize the use of semiconductor nanocrystals as fluorescent labels in biomedical tests.

For therapy, one might encapsulate drugs within nanometer-scale packages that control the medicines' release in sophisticated ways.

but they emit light only at one specific wavelength, corresponding to the band-gap energy. Quantum dots are an intermediate case. Like bulk semiconductors, they absorb photons of all energies above the threshold of the band gap. But the wavelength of light a quantum dot emits—its color—depends very strongly on the dot's size. Hence, a single type of semiconducting material can yield an entire family of distinctly colored labels.

Physicists first studied quantum dots in the 1970s, thinking that they might one day fashion new electronic or optical devices. Few of the pioneering investigators had any idea that these objects could help diagnose disease or discover new

drugs. And none of them would have dreamed that the first real-world applications of quantum dots would be in biology and medicine. Making quantum dots that would function properly in biological systems did indeed require years of research, but they are now a reality.

The Rainbow Coalition

THE COMPANY LEADING the push to commercialize this technology, Quantum Dot Corporation, has licensed techniques developed in my lab and at the Massachusetts Institute of Technology, Indiana University, Lawrence Berkeley National Laboratory and the University of Melbourne in Australia. I helped to found this company, so my assessments may be biased, but I view the prospects for quantum dots as, well, bright.

Semiconductor nanocrystals have several advantages over conventional dye molecules. Small inorganic crystals can withstand significantly more cycles of excitation and light emission than can typical organic molecules, which soon decompose. And this stability allows investigators to track the goings-on in cells and tissues for longer intervals than can now be achieved. But the greatest benefit semiconductor nanocrystals offer is less subtle—they come in more colors.

Biological systems are very complex, and frequently several components must be observed simultaneously. Such tracking is difficult to achieve, because each organic dye must be excited with a different wavelength of light. But quantum dots make it possible to tag a variety of biological molecules, each with a crystal of a different size (and hence color). And because all of these crystals can be energized with a single light source, they can all be monitored at once.

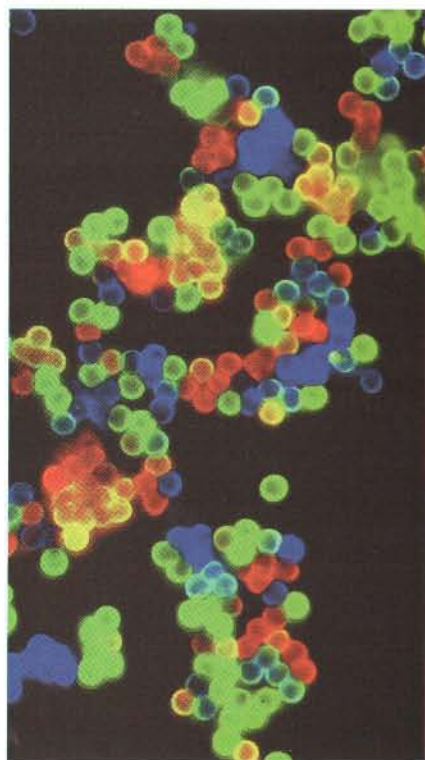
This approach is being pursued actively, but quantum dots offer even more interesting possibilities. Imagine a small latex bead filled with a combination of quantum dots. The bead could, for in-

stance, contain five different sizes of dots, or five colors, in a variety of concentrations. After the bead is illuminated, it will give off light, which when spread out by a prism will produce five distinct spectral lines with prescribed intensities—a spectral bar code, if you like. Such beads allow for an enormous number of distinct labels (billions, potentially), each of which could be attached, say, to DNA molecules composed of different sequences of genetic building blocks.

With these kinds of beads, technicians could easily compare the genetic material in a sample against a library of known DNA sequences, as might be done if an investigator wanted to find out which genes were active in certain cells or tissues. They would simply expose the sample to the full beaded library and read the spectral bar codes of the library DNAs that bind to sequences in the sample. Because binding takes place only when genetic sequences match closely (or more precisely, when one sequence complements the other), the results would immediately reveal the nature of the genetic material in the sample.

Semiconductor quantum dots should soon serve biomedical researchers in this way, but they are not the only nanostructures useful for optically sensing the genetic composition of biological specimens. Another example emerges from the work of Chad A. Mirkin and Robert L. Letsinger of Northwestern University, who recently developed an ingenious method to test for the presence of a specific genetic sequence in solution. Their scheme employs 13-nanometer gold particles studded with DNA.

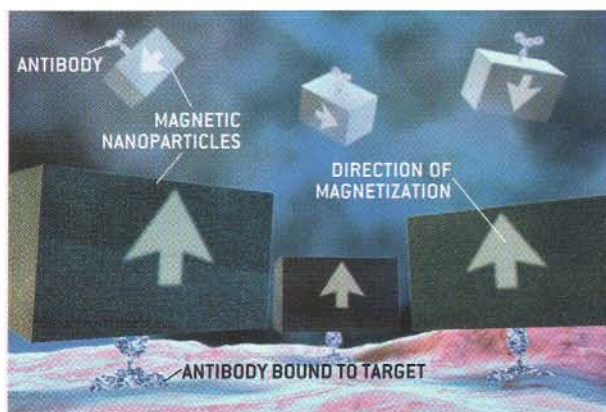
The trick here is to use two sets of gold particles. The first set carries DNA that binds to one half of the target sequence; the second set carries DNA that binds to the other half. DNA with the complete target sequence readily attaches to both types of particles, linking them together. Because each particle has mul-



LATEX BEADS filled with quantum dots of single colors glow at nearly the same wavelengths as the dots themselves. Researchers have also loaded selections of different dots into single beads. Their aim is to create a huge variety of distinct labels for biological tests. [See also "Nano Bar Codes" in the box on the opposite page.]

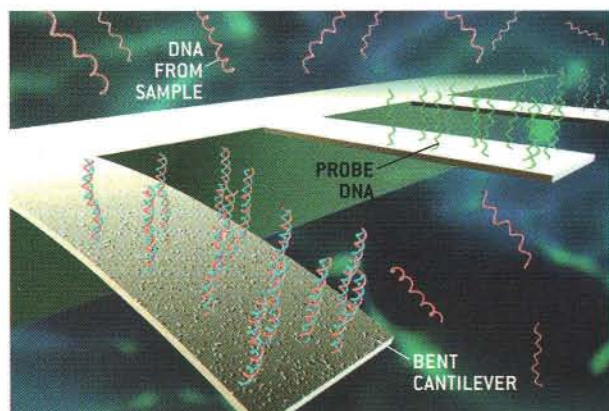
BIO-NANOTECH IN ACTION

The items here could one day enhance the speed and power of biomedical tests, such as those used to screen small samples of material for the presence of particular genetic sequences. For clarity, the images have not been drawn to scale.



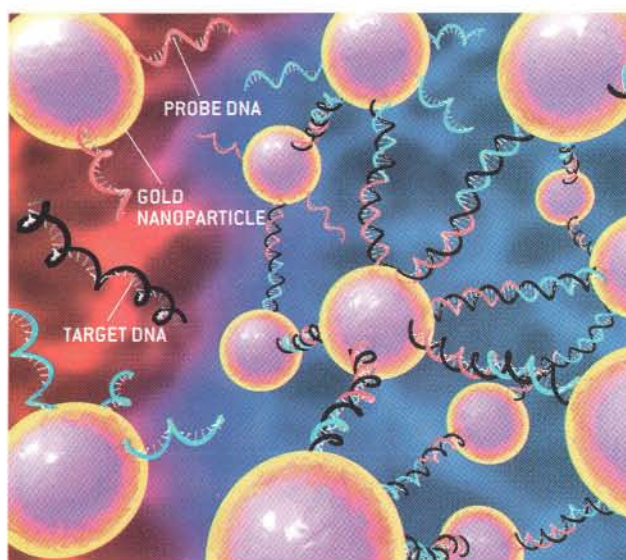
MAGNETIC TAGS

Many tests reveal the presence of a molecule or disease-causing organism by detecting the binding of an antibody to that target. When antibodies labeled with magnetic nanoparticles bind to their target on a surface (*foreground*), brief exposure to a magnetic field causes these probes collectively to give off a strong magnetic signal. Meanwhile unbound antibodies tumble about in all directions, producing no net signal. This last property makes it possible to read the results without first washing away any probes that fail to find their target.



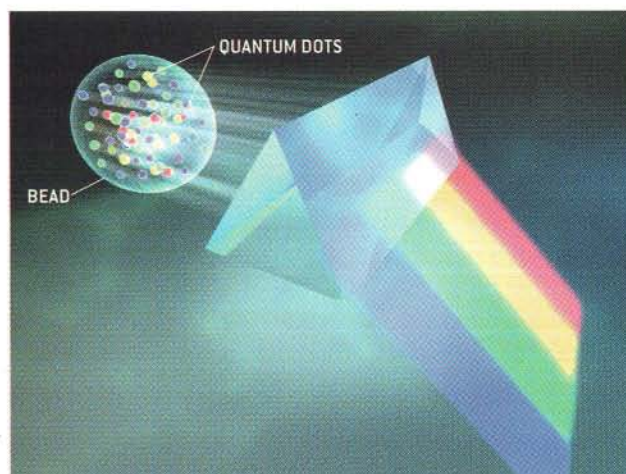
CLEVER CANTILEVERS

Biological samples can be screened for the presence of particular genetic sequences using small beams (cantilevers) of the type employed in atomic force microscopes. The surface of each cantilever is coated with DNA able to bind to one particular target sequence. A sample is then applied to the beams. Binding induces a surface stress, which bends the affected beams by nanometers—not much, but enough to reveal that the bent beams found their specific targets in a sample.



GOLD PARTICLES

Gold nanoparticles studded with short segments of DNA could form the basis of an easy-to-read test for the presence of a genetic sequence (*black*) in a sample under study. DNA complementary to half of such a sequence (*red*) is attached to one set of particles in solution, and DNA complementary to the other half (*blue*) is attached to a second set of particles. If the sequence of interest is present in the sample, it will bind to the DNA tentacles on both sets of spheres, trapping the balls in a dense web. This agglomeration will cause the solution to change color (*from red to blue*).



NANO BAR CODES

Latex beads filled with several colors of nanoscale semiconductors known as quantum dots can potentially serve as unique labels for any number of different probes. In response to light, the beads would identify themselves (and, thus, their linked probes) by emitting light that separates into a distinctive spectrum of colors and intensities—a kind of spectral bar code.

multiple DNA tentacles, bits of genetic material carrying the target sequence can glue many particles together. And when these gold specks aggregate, their optical properties shift markedly, changing the test solution from red to blue. Because the outcome of the test is easy to see without any instrumentation at all, such a system might be particularly useful for home DNA testing.

Feeling the Force

NO DISCUSSION of bio-nanotechnology would be complete without at least a brief mention of one of the hottest instruments in science today—the atomic force microscope. Such devices probe materials in the same way an old-fashioned phonograph reads the grooves in a record: by dragging a sharp point over the surface and detecting the resulting deflections. The tip of an atomic force microscope is, however, much finer than a phonograph needle, so it can sense far smaller structures. Regrettably, fabricating tips that are both fine and sturdy for

these microscopes has proved to be quite difficult.

The solution appeared in 1996, when workers at Rice University affixed a slender carbon nanotube to the tip of an atomic force microscope, making it possible to probe samples just a few nanometers in size. In 1998 Charles M. Lieber and his co-workers at Harvard University applied this approach to probing biomolecules, providing a very high resolution means to explore complex biological molecules and their interactions at the most basic level.

But atomic force microscopy may soon be applied to more than just making fundamental scientific measurements. Last year James K. Gimzewski, then at the IBM Zurich Research Laboratory, showed with collaborators at IBM and the University of Basel that an array of micron-scale arms, or cantilevers, much like the ones employed in atomic force microscopes, could be used to screen samples for the presence of certain genetic sequences. They attached short

strands of DNA to the tops of the cantilevers. When genetic material carrying a complementary sequence binds to the anchored strands, it induces a surface stress, which bends the cantilevers subtly—by just nanometers—but enough to be detected. By fabricating devices with many cantilevers and coating each with a different type of DNA, researchers should be able to test a biological sample rapidly for the presence of specific genetic sequences (as is now done routinely with gene chips) by nanomechanical means without the need for labeling.

This example, like the others described earlier, illustrates that the connections between nanotechnology and the practice of medicine are often indirect, in that much of the new work promises only better research tools or aids to diagnosis. But in some cases, nano-objects being developed may themselves prove useful for therapy. One might, for instance, encapsulate drugs within nanometer-scale packages that control the medicines' release in sophisticated ways.

Consider a class of artificial molecules called organic dendrimers. Two decades ago Donald A. Tomalia of the Michigan Molecular Institute in Midland fashioned the first of these intriguing structures. A dendrimer molecule branches successively from inside to outside. Its shape resembles what one would get by taking many sprigs from a tree and poking them into a foam ball so that they shot out in every direction. Dendrimers are globular molecules about the size of a typical protein, but they do not come apart or unfold as easily as proteins do, because they are held together with stronger chemical bonds.

Like the lush canopies of mature trees, dendrimers contain voids. That is, they have an enormous amount of internal surface area. Interestingly, they can be tailored to have a range of different cavity sizes—spaces that are just perfect for holding therapeutic agents. Dendrimers can also be engineered to transport DNA into cells for gene therapy, and they might work more safely than the other leading method: genetically modified viruses.

Other types of nanostructures pos-

Petite Plumbing Jobs

Microfluidics enhances biomedical research

Most of the nanotechnologies now being developed for biomedical use take the form of minute objects immersed in comparatively large quantities of fluid, be it water, blood or a complex experimental concoction. But investigators are also building devices to manipulate tiny amounts of such liquids. These so-called microfluidic systems pump solutions through narrow channels, controlling the flow with diminutive valves and intense electric fields.

The ability to handle vanishingly small quantities of a solution in this way allows biomedical researchers to carry out many different experiments on what might be only a modest amount of sample—and to do so in an efficient manner, with hundreds of tests being performed, say, on the surface of a single glass slide. Microfluidic devices also offer researchers the means to carry out experiments that could not otherwise be done; for example, to deliver test solutions of specific compositions to different parts of a cell under study.

Although many of the components being created for these systems are considerably larger than a micron, some experimental devices include nanoscale dimensions. Notably, Harold G. Craighead's team at Cornell University has devised methods for sorting different sizes of DNA fragments in water according to how fast the fragments traverse passages measuring 100 nanometers across or travel through microchannels that repeatedly narrow to a depth of 75 to 100 nanometers. These or other nanofluidic devices could potentially increase the speed and reduce the costs of separating DNA molecules for sequencing and could in theory be adapted for separating proteins or other molecules.

—A.P.A.

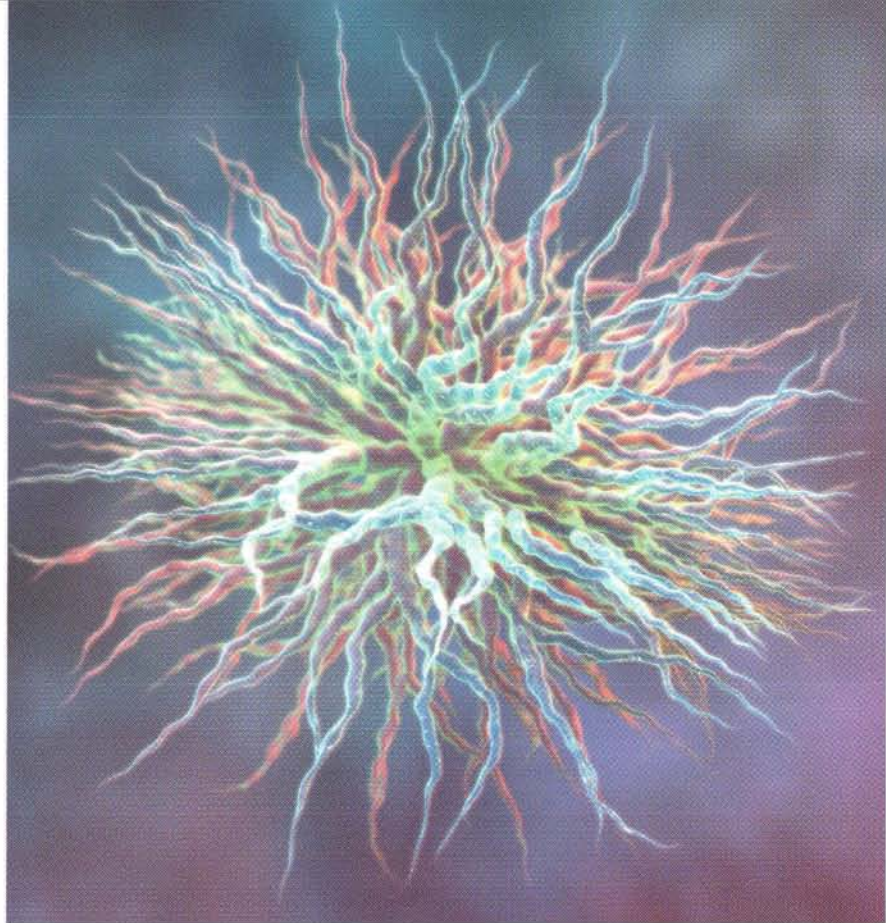
sess high surface area, and these too may prove useful for delivering drugs where they are needed. But dendrimers offer the greatest degree of control and flexibility. It may be possible to design dendrimers that spontaneously swell and liberate their contents only when the appropriate trigger molecules are present. This ability would allow a custom-made dendrimer to release its load of drugs in just the tissues or organs needing treatment.

Other drug-delivery vehicles on the horizon include hollow polymer capsules under study by Helmuth Möhwald of the Max Planck Institute of Colloids and Interfaces in Golm, Germany. In response to certain signals, these capsules swell or compress to release drugs. Also intriguing are so-called nanoshells, recently invented by the researchers at Rice.

Nanoshells are extremely small beads of glass coated with gold. They can be fashioned to absorb light of almost any wavelength, but nanoshells that capture energy in the near-infrared are of most interest because these wavelengths easily penetrate several centimeters of tissue. Nanoshells injected into the body can therefore be heated from the outside using a strong infrared source. Such a nanoshell could be made to deliver drug molecules at specific times by attaching it to a capsule made of a heat-sensitive polymer. The capsule would release its contents only when gentle heating of the attached nanoshell caused it to deform.

A more dramatic application envisioned for nanoshells is in cancer therapy. The idea is to link the gold-plated spheres to antibodies that bind specifically to tumor cells. Heating the nanoshells sufficiently would in theory destroy the cancerous cells, while leaving nearby tissue unharmed.

It is, of course, difficult to know for certain whether nanoshells will ultimately fulfill their promise. The same can be said for the myriad other minuscule devices being developed for medical use—among them, one-nanometer buckyballs made from just a few dozen carbon atoms. Yet it seems likely that some of the objects being investigated today will be serving doctors in the near future.



ORGANIC DENDRIMER, shown in an artist's conception, could be roughly the size of a protein molecule. Dendrimers harbor many internal cavities and are being eyed as drug-delivery vehicles.

Even more exciting is the prospect that physicians will make use of nanoscale building blocks to form larger structures, thereby mimicking the natural processes of biology. Such materials might eventually serve to repair damaged tissues. Research on these bold strategies is just beginning, but at least one enterprise already shows that the notion has merit: building scaffoldings on which to grow bone. Samuel I. Stupp of Northwestern is pioneering this approach using synthetic molecules that combine into fibers to which bone cells have a strong tendency to adhere.

What other marvels might the future hold? Although the means to achieve them are far from clear, sober nanotech-

nologists have stated some truly ambitious goals. One of the "grand challenges" of the National Nanotechnology Initiative is to find ways to detect cancerous tumors that are a mere few cells in size. Researchers also hope eventually to develop ways to regenerate not just bone or cartilage or skin but also more complex organs, using artificial scaffoldings that can guide the activity of seeded cells and can even direct the growth of a variety of cell types. Replacing hearts or kidneys or livers in this way might not match the fictional technology of *Fantastic Voyage*, but the thought that such medical therapies might actually become available in the not so distant future is still fantastically exciting. **SA**

MORE TO EXPLORE

Ultrasensitive Magnetic Biosensor for Homogeneous Immunoassay. Y. R. Chemla, H. L. Grossman, Y. Poon, R. McDermott, R. Stevens, M. D. Alper and J. Clarke in *Proceedings of the National Academy of Sciences USA*, Vol. 97, No. 27, pages 14268–14272; December 19, 2000.

The author's Web site is at www.cchem.berkeley.edu/~pagrp/

Information on using gold nanoparticles for DNA testing is available at www.chem.nwu.edu/~mknggrp/dnasubgr.html

Information on nanoshells is available at www.ece.rice.edu/~halas/

Information about quantum dots and their use in biomedicine is available at www.qdots.com

| By K. Eric Drexler

Machine-Phase Nanotechnology

A molecular nanotechnology pioneer predicts that the tiniest robots will revolutionize manufacturing and transform society

IN 1959 PHYSICIST Richard Feynman gave an after-dinner talk exploring the limits of miniaturization. He set out from known technology (at a time when an adding machine could barely fit in your pocket), surveyed the limits set by physical law and ended by arguing the possibility—even inevitability—of “atom by atom” construction.

What at the time seemed absurdly ambitious, even bizarre, has recently become a widely shared goal. Decades of technological progress have shrunk microelectronics to the threshold of the molecular scale, while scientific progress at the molecular level—especially on the

to put every atom in a selected place (where it would serve as part of some active or structural component) with no extra molecules on the loose to jam the works. Such a system would not be a liquid or gas, as no molecules would move randomly, nor would it be a solid, in which molecules are fixed in place. Instead this new machine-phase matter would exhibit the molecular movement seen today only in liquids and gases as well as the mechanical strength typically associated with solids. Its volume would be filled with active machinery.

The ability to construct objects with molecular precision will revolutionize

molecular repair of the human body. Medical nanorobots are envisioned that could destroy viruses and cancer cells, repair damaged structures, remove accumulated wastes from the brain and bring the body back to a state of youthful health.

Another surprising medical application would be the eventual ability to repair and revive those few pioneers now in suspended animation (currently regarded as legally deceased), even those who have been preserved using the crude cryogenic storage technology available since the 1960s. Today’s vitrification techniques—which prevent the forma-

In principle, Drexler says, a molecular construction system called
an assembler could build almost anything, including copies of itself.

molecular machinery of living systems—has now made clear to many what was envisioned by a sole genius so long ago.

Inspired by molecular biology, studies of advanced nanotechnologies have focused on bottom-up construction, in which molecular machines assemble molecular building blocks to form products, including new molecular machines. Biology shows us that molecular machine systems and their products can be made cheaply and in vast quantities.

Stepping beyond the biological analogy, it would be a natural goal to be able

manufacturing, permitting materials properties and device performance to be greatly improved. In addition, when a production process maintains control of each atom, there is no reason to dump toxic leftovers into the air or water. Improved manufacturing would also drive down the cost of solar cells and energy storage systems, cutting demand for coal and petroleum, further reducing pollution. Such advances raise hope that those in the developing world will be able to reach First World living standards without causing environmental disaster.

Low-cost, lightweight, extremely strong materials would make transportation far more energy efficient and—finally—make space transportation economical. The old dreams of expanding the biosphere beyond our one vulnerable planet suddenly look feasible once more.

Perhaps the most exciting goal is the

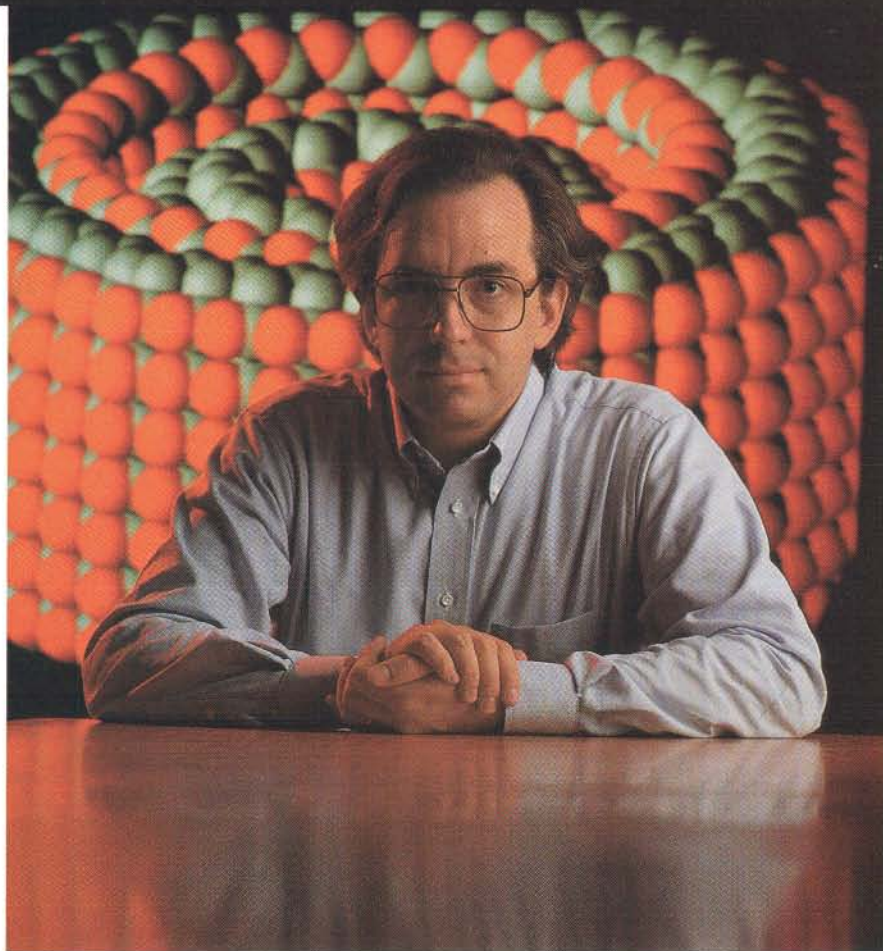
tion of damaging ice crystals—should make repair easier, but even the original process appears to preserve brain structure well enough to enable restoration.

Those researchers most familiar with the field of molecular nanotechnology see the technology base underpinning such capabilities as perhaps one to three decades off. At the moment, work focuses on the earliest stages: finding out how to build larger structures with atomic precision, learning to design molecular machines and identifying intermediate goals with high payoff.

To understand the potential of molecular manufacturing technology, it helps to look at the macroscale machine systems used now in industry. Picture a robotic arm that reaches over to a conveyor belt, picks up a loaded tool, applies the tool to a workpiece under construction, replaces the empty tool on the belt,

ABOUT THE AUTHOR

K. ERIC DREXLER is chairman of the Foresight Institute, research fellow of the Institute for Molecular Manufacturing, and author of *Engines of Creation* and *Nanosystems: Molecular Machinery, Manufacturing, and Computation*.



picks up the next loaded tool, and so on—as in today’s automated factories.

Now mentally shrink this entire mechanism, including the conveyor belt, to the molecular level to form an image of a nanoscale construction system. Given a sufficient variety of tools, this system would be a general-purpose building device, nicknamed an assembler. In principle, it could build almost anything, including copies of itself.

Molecular nanotechnology as a field does not depend on the feasibility of this particular proposal—a collection of less general building devices could carry out the functions mentioned above. But because the assembler concept is still controversial, it’s worth mentioning the objections being raised.

One prominent chemist speaking at a recent event sponsored by the American Association for the Advancement of Science asked how one could power and direct an assembler and whether it could really break and re-form strong molecular bonds. These are reasonable questions that can be answered only by de-

NANOSCRIBE K. Eric Drexler conceived the concept of molecular machine systems [a component of one is shown in the background].

scribing designs and calculations too bulky to fit in this essay. Fortunately, technical literature providing seemingly adequate answers has been available since at least 1992, when my book *Nanosystems* was published.

Another well-known chemist objects that an assembler would need 10 robotic “fingers” to carry out its operations and that there isn’t room for them all. The need for such a large number of manipulators, however, has never been established or even seriously argued. In contrast, the designs that have received (and survived) the most peer review use one tool at a time and grip their tools without using any fingers at all.

These examples point to the difficulty of finding appropriate critiques of nanotechnology designs. Many researchers whose work seems relevant are actually the wrong experts—they are excellent in their discipline but have little expertise in

systems engineering. The shortage of molecular systems engineers will probably be a limiting factor in the speed with which nanotechnology can be developed.

It is important that critiques of nanotechnology are well executed, because vital societal decisions depend on them. If molecular nanotechnology as described here is correct, policy issues can look quite different from what is generally expected. Today most people believe that global warming will be hard to correct—with nanotechnology, excess greenhouse gases could be inexpensively removed from the atmosphere. Current Social Security projections assume increasing numbers of aged citizens in poor health. With advanced medical nanotechnology, tomorrow’s seniors could be more active and healthy than they are now, bringing new meaning to the “golden years.”

Likewise, we need to focus now on avoiding accidents and preventing abuse of this powerful technology. Solid work has been done on the problem of heading off major nanotechnology accidents. The Foresight Guidelines, available on the World Wide Web, sketch out proposed safety rules [see below].

But the challenge of preventing abuse—the exploitation of this technology by aggressive governments, terrorist groups or even individuals for their own purposes—still looms large. The closest analogy to this problem these days is the difficulty of controlling the proliferation of chemical and biological weapons. The advance toward molecular nanotechnology highlights the urgency in finding effective ways to manage emerging technologies that are powerful, valuable and open to misuse.

MORE TO EXPLORE

Engines of Creation: The Coming Era of Nanotechnology. K. E. Drexler. Fourth Estate, 1990.

Nanosystems: Molecular Machinery, Manufacturing, and Computation. K. E. Drexler. John Wiley & Sons, 1992.

The Foresight Institute and the Foresight Guidelines: www.foresight.org

Richard Feynman’s lecture “There’s Plenty of Room at the Bottom” can be found at www.zyvex.com/nanotech/feynman.html

By Richard E. Smalley

Of Chemistry, Love and Nanobots

How soon will we see the nanometer-scale robots envisaged by K. Eric Drexler and other molecular nanotechologists? The simple answer is never

WHEN A BOY AND A GIRL fall in love, it is often said that the chemistry between them is good. This common use of the word "chemistry" in human relations comes close to the subtlety of what actually happens in the more mundane coupling of molecules. In a chemical reaction between two "consenting" molecules, bonds form between some of the atoms in what is usually a complex dance involving motion in multiple dimensions. Not just any two molecules will react. They have to be right for each other. And if the chemistry is really, really good, the molecules that do react will all produce the exact product desired.

cramped region of space measuring no more than a nanometer on each side.

In recent years, it has become popular to imagine tiny robots (sometimes called assemblers) that can manipulate and build things atom by atom. Imagine a single assembler: working furiously, this hypothetical nanorobot would make many new bonds as it went about its assigned task, placing perhaps up to a billion new atoms in the desired structure every second. But as fast as it is, that rate would be virtually useless in running a nanofactory: generating even a tiny amount of a product would take a solitary nanobot millions of years. (Making

certainly build another copy of itself. It could therefore self-replicate, much as biological cells do. After a while, we'd have a second nanobot and, after a little more time, four, then eight, then 16 and so on.

For fun, suppose that each nanobot consisted of a billion atoms (10^9 atoms) in some incredibly elaborate structure. If these nanobots could be assembled at the full billion-atoms-per-second rate imagined earlier, it would take only one second for each nanobot to make a copy of itself. The new nanobot clone would then be "turned on" so that it could start its own reproduction. After 60 seconds

Manipulator fingers on the hypothetical self-replicating nanobot are not only too fat; they are also too sticky.

Both these problems are fundamental, and neither can be avoided.

Near the center of the typical chemical reaction, the particular atoms that are going to form the new bonds are not the only ones that jiggle around: so do all the atoms they are connected to and the ones connected to these in turn. All these atoms must move in a precise way to ensure that the result of the reaction is the one intended. In an ordinary chemical reaction five to 15 atoms near the reaction site engage in an intricate three-dimensional waltz that is carried out in a

a mole of something—say, 30 grams, or about one ounce—would require at least 6×10^{23} bonds, one for each atom. At the frenzied rate of 10^9 per second it would take this nanobot 6×10^{14} seconds—that is, 10^{13} minutes, which is 6.9×10^9 days, or 19 million years.) Although such a nanobot assembler would be very interesting scientifically, it wouldn't be able to make much on its own in the macroscopic "real" world.

Yet imagine if this one nanobot were so versatile that it could build anything, as long as it had a supply of the right kinds of atoms, a source of energy and a set of instructions for exactly what to build. We could work out these detailed instructions with a computer and then radio them to the nanobot. If the nanobot could really build anything, it could

of this furious cloning, there would be 2^{60} nanobots, which is the incredibly large number of 1×10^{18} , or a billion billion. This massive army of nanobots would produce 30 grams of a product in 0.6 millisecond, or 50 kilograms per second. Now we're talking about something very big indeed!

Nanobots in general may not be terribly interesting as a way of making prodigious amounts of things, but self-replicating nanobots are really interesting. If they are feasible, then the notion of a machine that can build anything from a CD player to a skyscraper in a remarkably short time doesn't seem so far-fetched.

But these self-replicating nanobots can also be quite scary. Who will control them? How do we know that some sci-

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entist or computer hacker won't design one that is truly autonomous, carrying a complete set of instructions for itself? How do we know that these nanobots won't mutate and that some of these mutants won't achieve the ability, like cancer cells, to disregard any signals that would otherwise trigger self-destruction? How could we stop them once they reached this malignant state? Self-replicating nanobots would be the equivalent of a new parasitic life-form, and there might be no way to keep them from expanding indefinitely until everything on earth became an undifferentiated mass of gray goo.

Still more frightening, they would by either design or random mutation develop the ability to communicate with one another. Maybe they would form groups, constituting a primitive nervous system. Perhaps they would really become "alive" by any definition of that term. Then, in the memorable words of Bill Joy, the chief scientist at Sun Microsystems and

someone who has worried in print about the societal implications of proliferating nanobots, the future simply would not need us.

But how realistic is this notion of a self-replicating nanobot? Let's think about it. Atoms are tiny and move in a defined and circumscribed way—a chemist would say that they move so as to minimize the free energy of their local surroundings. The electronic "glue" that sticks them to one another is not local to each bond but rather is sensitive to the exact position and identity of all the atoms in the near vicinity. So when the nanomanipulator arm of our nanobot picks up an atom and goes to insert it in the desired place, it has a fundamental problem. It also has to somehow control not only this new atom but all the existing atoms in the region. No problem, you say: our nanobot will have an addi-

NOBELIST Richard E. Smalley dismisses the notion of out-of-control nanorobots.

tional manipulator arm for each one of these atoms. Then it would have complete control of all the goings-on that occur at the reaction site.

But remember, this region where the chemistry is to be controlled by the nanobot is very, very small—about one nanometer on a side. That constraint leads to at least two basic difficulties. I call one the fat fingers problem and the other the sticky fingers problem. Because the fingers of a manipulator arm must themselves be made out of atoms, they have a certain irreducible size. There just isn't enough room in the nanometer-size reaction region to accommodate all the fingers of all the manipulators necessary to have complete control of the chemistry. In a famous 1959 talk that has inspired nanotechnologists everywhere, Nobel physicist Richard Feynman memorably noted, "There's plenty of room at the bottom." But there's not *that* much room.

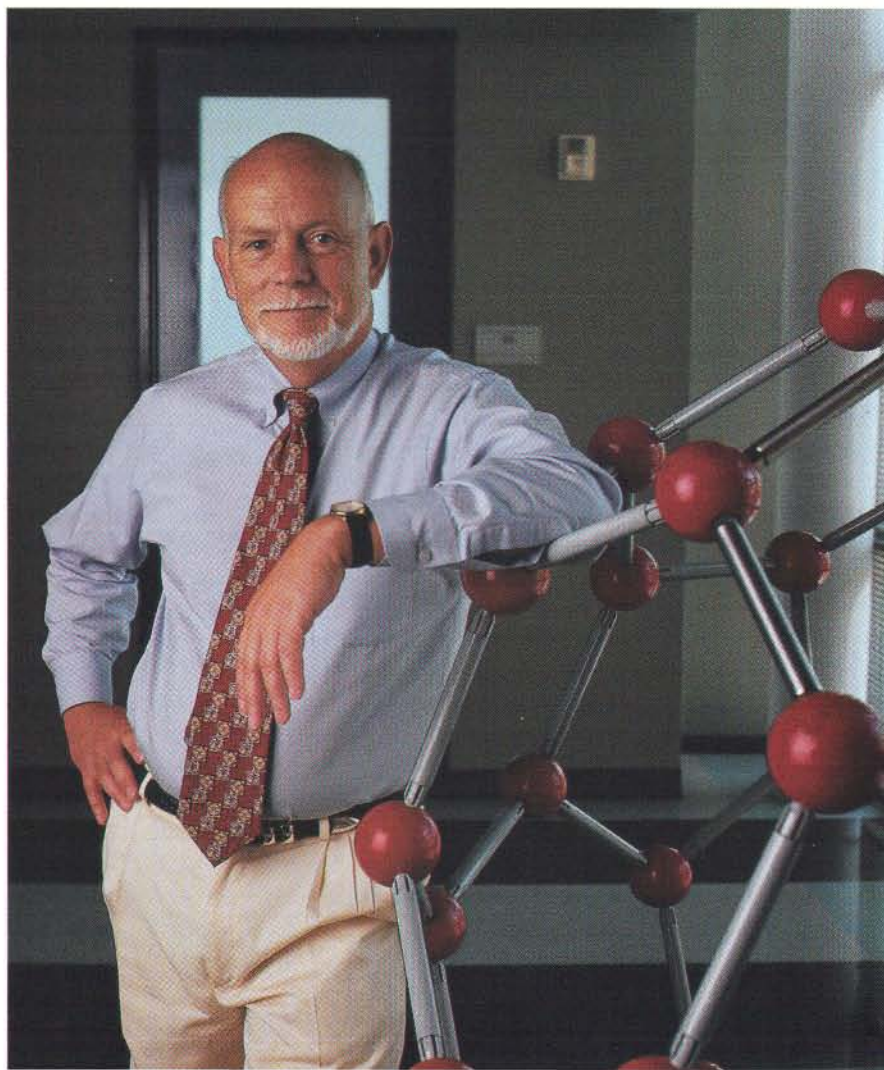
Manipulator fingers on the hypothetical self-replicating nanobot are not only too fat; they are also too sticky: the atoms of the manipulator hands will adhere to the atom that is being moved. So it will often be impossible to release this minuscule building block in precisely the right spot.

Both these problems are fundamental, and neither can be avoided. Self-replicating, mechanical nanobots are simply not possible in our world. To put every atom in its place—the vision articulated by some nanotechnologists—would require magic fingers. Such a nanobot will never become more than a futurist's daydream.

Chemistry is subtle indeed. You don't make a girl and a boy fall in love by pushing them together (although this is often a step in the right direction). Like the dance of love, chemistry is a waltz with its own step-slide-step in three-quarter time. Wishing that a waltz were a merengue—or that we could set down each atom in just the right place—doesn't make it so.

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| By George M. Whitesides

The Once and Future Nanomachine

Biology outmatches futurists' most elaborate fantasies for molecular robots

AMONG THE PROMISED FRUITS of nanotechnology, small machines have always stood out. Their attraction is straightforward. Large machines—airplanes, submarines, robotic welders, toaster ovens—are unquestionably useful. If one could take the same ideas used to design these devices and apply them to machines that were a tiny fraction of their size, who knows what they might be able to do?

Imagining two types of small machines—one analogous to an existing machine, the second entirely new—has captured broad attention. The first is a nanoscale submarine, with dimensions of only a few billionths of a meter—the

ering its ultimate practicality). It would be a new type of machine—a universal fabricator. It would make any structure, including itself, by atomic-scale “pick and place”: a set of nanoscale pincers would pick individual atoms from their environment and place them where they should go. The Drexlerian vision imagines society transformed forever by small machines that could create a television set or a computer in a few hours at essentially no cost. It also has a dark side. The potential for self-replication of the assembler has raised the prospect of what has come to be called gray goo: myriads of self-replicating nanoassemblers making un-

commonly considered to be the products of human design and intention, why shouldn't a complex molecular system that performs a function also be considered a machine, even if it is the product of evolution rather than of design?

Issues of teleology aside, and accepting this broad definition, nanoscale machines already do exist, in the form of the functional molecular components of living cells—such as molecules of protein or RNA, aggregates of molecules, and organelles (“little organs”)—in enormous variety and sophistication. The broad question of whether nanoscale machines exist is thus one that was answered in the

The charm of the assembler is illusory:

it is more appealing as metaphor than as reality, and less the solution of a problem than the hope for a miracle.

length of a few tens or hundreds of atoms. This machine might, so the argument goes, be useful in medicine by navigating through the blood, seeking out diseased cells and destroying them.

The second—the so-called assembler—is a more radical idea, originally proposed by futurist K. Eric Drexler. This machine has no macroscopic analogue (a fact that is important in consid-

countable copies of themselves and ravaging the earth while doing so).

Does the idea of nanoscale machines make sense? Could they be made? If so, would they be effectively downsized versions of their familiar, large-scale cousins, or would they operate by different principles? Might they, in fact, ravage the earth?

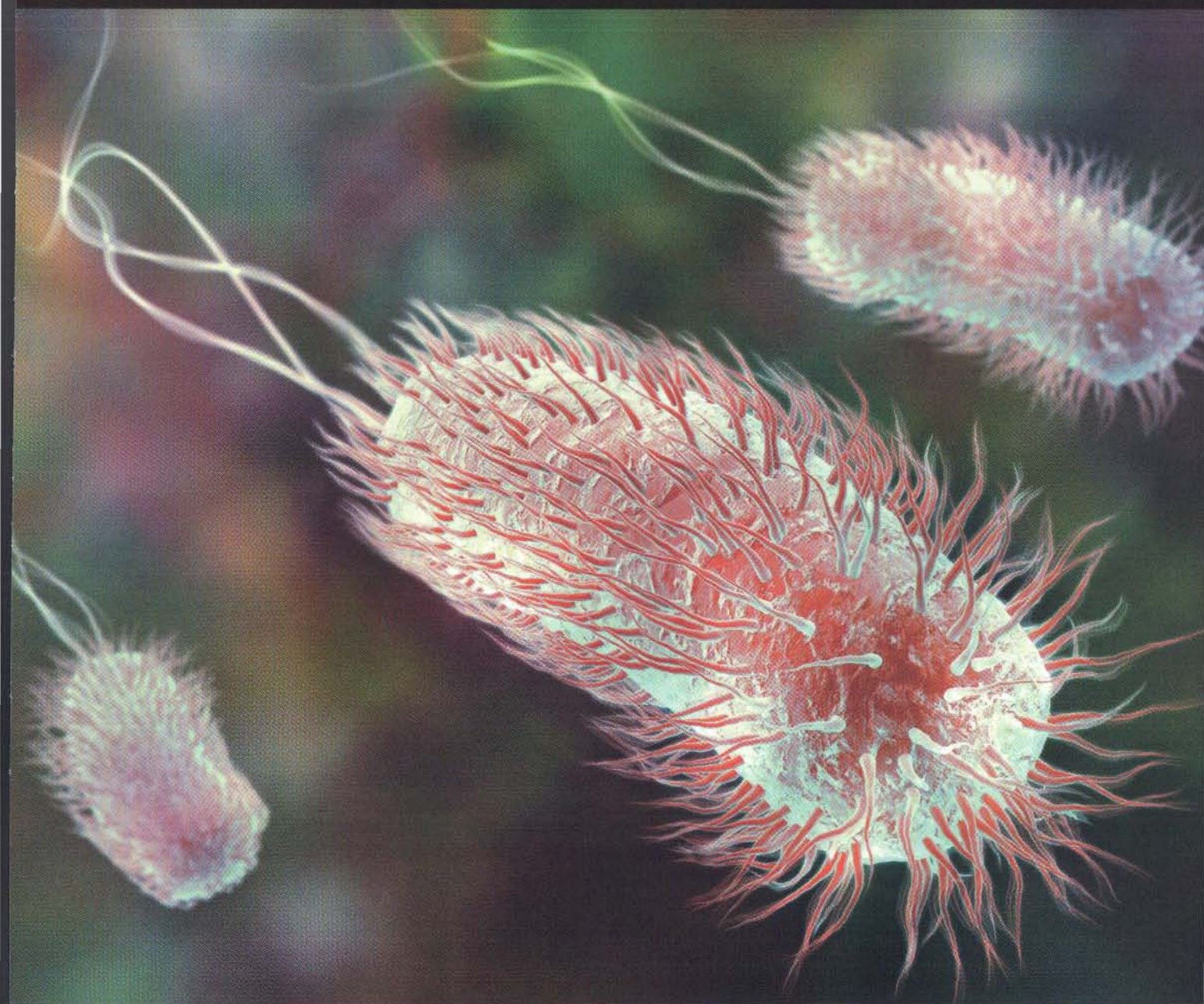
We can begin to answer these intriguing questions by asking a more ordinary one: What is a machine? Of the many definitions, I choose to take a machine to be “a device for performing a task.” Going further, a machine has a design; it is constructed following some process; it uses power; it operates according to information built into it when it is fabricated. Although machines are

affirmative by biologists many years ago. The question now is: What are the most interesting designs to use for *future* nanomachines? And what, if any, risks would they pose?

Cells include some molecular machines that seem similar to familiar human-scale machines: a rotary motor fixed in the membrane of a bacterium turns a shaft and superficially resembles an electric motor. Others more loosely resemble the familiar: an assembly of RNA and protein—the ribosome—makes proteins by an assembly line-like process. And some molecular machines have no obvious analogy in macroscopic machines: a protein—topoisomerase—unwinds double-stranded DNA when it becomes too tightly wound. The way in which these

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organelles are fabricated in the cell—an efficient synthesis of long molecules, combined with molecular self-assembly—is a model for economy and organization, and entirely unlike the brute-force method suggested for the assembler.

And as for ravaging the earth: in a sense, collections of biological cells already *have* ravaged the earth. Before life emerged, the planet was very different from the way it is today. Its surface was made of inorganic minerals; its atmosphere was rich in carbon dioxide. Life rapidly and completely remodeled the planet: it contaminated the pristine surface with microorganisms, plants and or-

ganic materials derived from them; it largely removed the carbon dioxide from the atmosphere and injected enormous quantities of oxygen. Overall, a radical change. Cells—self-replicating collections of molecular nanomachines—completely transformed the surface and the atmosphere of our planet. We do not normally think of this transformation as “ravaging the planet,” because we thrive in the present conditions, but an outside observer might have thought otherwise.

So the issue is not whether nanoscale machines can exist—they already do—or whether they can be important—we often consider ourselves as demonstrations

WHIPLIKE TAILS, found on many bacteria, are propelled by nanomotors. The tiny biochemical motor turns a rotary shaft that spins the tails, or flagella, and allows the bacteria, such as these *E. coli*, to move through liquid.

that they are—but rather where we should look for new ideas for design. Should we be thinking about the General Motors assembly line or the interior of a cell of *E. coli*? Let’s begin by comparing biological nanomachines—especially the ultimate self-replicating biological system, the cell—with nanoscale machines modeled on the large machines that now surround us. How does the bi-

ological strategy work, and how would it compare with a strategy based on making nanoscale versions of existing machines, or a new strategy of the type suggested by the assembler?

Molecular Copy Machines

THE CELL is a self-replicating structure. It takes in molecules from its environment, processes some of them for fuel, and reworks others into the pieces it uses to make, maintain, move and defend itself. DNA stores the information needed for fabrication and operation from one generation to the next. One kind of RNA (messenger RNA, or mRNA) serves as the temporary transcript of this information, "telling" ribosomes which protein to make. Membranes provide compartments that enclose the working parts, house portals that control the flux of molecules into and out of the cell, and hold molecules that sense the cell's environment. Proteins (often cooperating with other molecules) build everything in the cell and move its parts when they must be moved.

The strategy adopted by the cell to make its parts—and thus to replicate and maintain itself—is based on two ideas. The first is to use a single, conceptually

straightforward chemical process—polymerization—to create large, linear molecules. The second is to build molecules that spontaneously fold themselves into functional, three-dimensional structures. This two-part strategy does not require a difficult and sophisticated three-dimensional pick-and-place fabrication: it simply strings beads (for example, amino acids) together into a necklace (a polypeptide) and lets the necklace self-assemble into a machine (a protein). Thus, the information for the final, functional, three-dimensional structure is coded in the sequence of the beads. The three most important classes of molecules in the cell—DNA, RNA and proteins—are all made by this strategy; the proteins then make the other molecules in the cell. In many instances proteins also spontaneously associate with other molecules—proteins, nucleic acids, small molecules—to form larger functional structures. As a strategy for building complex, three-dimensional structures, this method of linear synthesis followed by various levels of molecular self-assembly is probably unbeatable for its efficiency.

The cell is, in essence, a collection of catalysts (molecules that cause chemical reactions to occur without themselves

being consumed) and other functional species—sensors, structural elements, pumps, motors. Most of the nanomachines in the cell are thus, ultimately, molecular catalysts. These catalysts do most of the work of the cell: they form the lipids (fats, for instance) that in turn self-assemble into the flexible sheet that encloses the cell; they make the molecular components necessary for self-replication; they produce the power for the cell and regulate its power consumption; they build archival and working information storage; and they maintain the interior environment within the proper operating parameters.

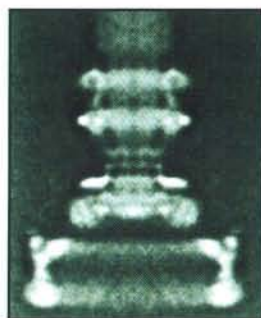
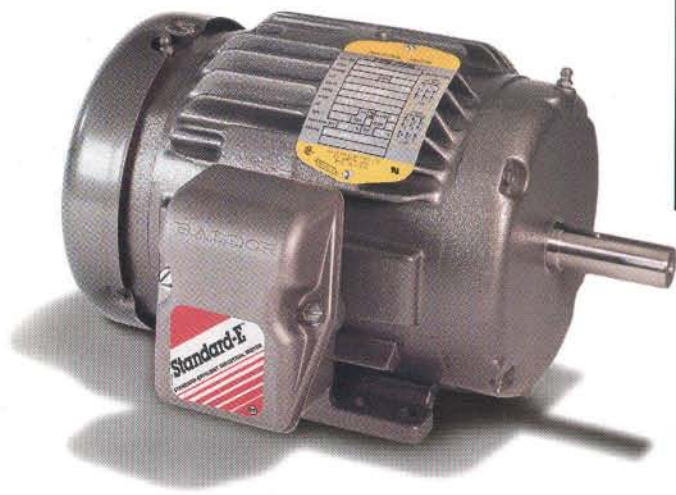
Among the many marvelous molecular machines employed by the cell, four are favorites of mine. The ribosome, made of ribosomal RNA (rRNA) and protein, is a key: it stands at the junction between information and action—between nucleic acids and proteins. It is an extraordinarily sophisticated machine that takes the information present in mRNA and uses it to build proteins.

The chloroplast, present in plant cells and algae, is a large structure that contains arrays of molecules that act as tuned optical antennas, collect photons from sunlight and employ them to generate chemical fuel that can be stored in the cell to power its many operations. The chloroplast, incidentally, also converts water to the oxygen that so contaminated the atmosphere when life first emerged: the stuff on which our lives depend was originally a waste product of cellular light-harvesting!

The mitochondrion is the power station: it carries out controlled combustion of organic molecules present in the cell—typically glucose—and generates power for the system. Instead of pumping electrons through wires to run electric motors, it generates molecules of ATP that move through the cell by diffusion and that are essential contributors to many biological reactions.

The flagellar motor of bacteria is a specialized but particularly interesting nanomachine, because it seems so similar to human-scale motors. The flagellar motor is a highly structured aggregate of proteins anchored in the membrane of

A TALE OF TWO MOTORS



STANDARD-ISSUE electric motor bears a superficial—albeit striking—resemblance to the biochemical rotary motor (top right) that turns the flagella in a bacterium.

many bacterial cells that provides the rotary motion that turns the flagella—the long whiplike structures that act as the propeller for these cells and allow them to propel themselves through water. It has a shaft, like an electric motor, and a structure around the shaft, like the ar-

large ratios of surface to volume, surface effects—both good and bad—become much more important for them than for large devices. Some of these types of problems will eventually be resolved if it is worthwhile to do so, but they provide difficult technical challenges now. We

The assembler, with its pick-and-place pincers, eliminates the many difficulties of fabricating nanomachines and of self-replication by ignoring them: positing a machine that can make any composition and any structure by simply placing atoms one at a time dismisses the

Considering the many constraints on the construction and operation of nanomachines, it seems that new systems for building them might ultimately look much like the ancient systems of biology.

mature of a motor. The similarity between flagellar and electrical motors is, however, largely illusory. The flagellar motor does not act by using electric current to generate moving magnetic fields; instead it uses the decomposition of ATP to cause changes in the shape of the molecules that, when combined with a sophisticated molecular ratchet, make the protein shaft revolve.

Nanomachines That Mimic Human-Scale Machines

CAN WE EVER APPROACH the elegant efficiency of cellular nanomachines by creating tiny cousins of the larger machines we have invented? Microfabrication has developed as an extraordinarily successful technology for manufacturing small, electronically functional devices—transistors and the other components of chips. Application of these techniques to simple types of machines with moving parts—mechanical oscillators and movable mirrors—has been technically successful. The development of these so-called microelectromechanical systems (MEMS) is proceeding rapidly, but the functions of the machines are still elementary, and they are micro, not nano, machines. The first true nanoscale MEMS (NEMS, or nanoelectromechanical systems) have been built only in the past few years and only experimentally [see “Plenty of Room, Indeed,” on page 42].

Many interesting problems plague the fabrication of nanodevices with moving parts. A crucial one is friction and sticking (sometimes combined in talking about small devices in the term “stiction”). Because small devices have very

will undoubtedly progress toward more complex micromachines and nanomachines modeled on human-scale machines, but we have a long path to travel before we can produce nanomechanical devices in quantity for any practical purpose. Nor is there any reason to assume that nanomachines must resemble human-scale machines.

Could these systems self-replicate? At present, we do not know how to build self-replicating machines of *any* size or type. We know, from recent biological studies, something about the minimum level of complexity in a living cell that will sustain self-replication: a system of some 300 genes is sufficient for self-replication. We have little sense for how to translate this number into mechanical machines of the types more familiar to us, and no sense of how to design a self-sustaining, self-replicating system of machines. We have barely taken the first steps toward self-replication in nonbiological systems [see “Go Forth and Replicate,” by Moshe Sipper and James A. Reggia; *SCIENTIFIC AMERICAN*, August].

And other problems cast long shadows. Where is the power to come from for an autonomous nanomachine? There are no electric sockets at the nanoscale. The cell uses chemical reactions of specific compounds to enable it to go about its business; a corresponding strategy for nanoscale machines remains to be developed. How would a self-replicating nanomachine store and use information? Biology has demonstrated a strategy based on DNA, so it can be done, but if one wanted a different strategy, it is not clear where to start.

most vexing aspects of fabrication. The assembler seems, however, from the vantage of a chemist, to be unworkable. Consider just two of the constraints.

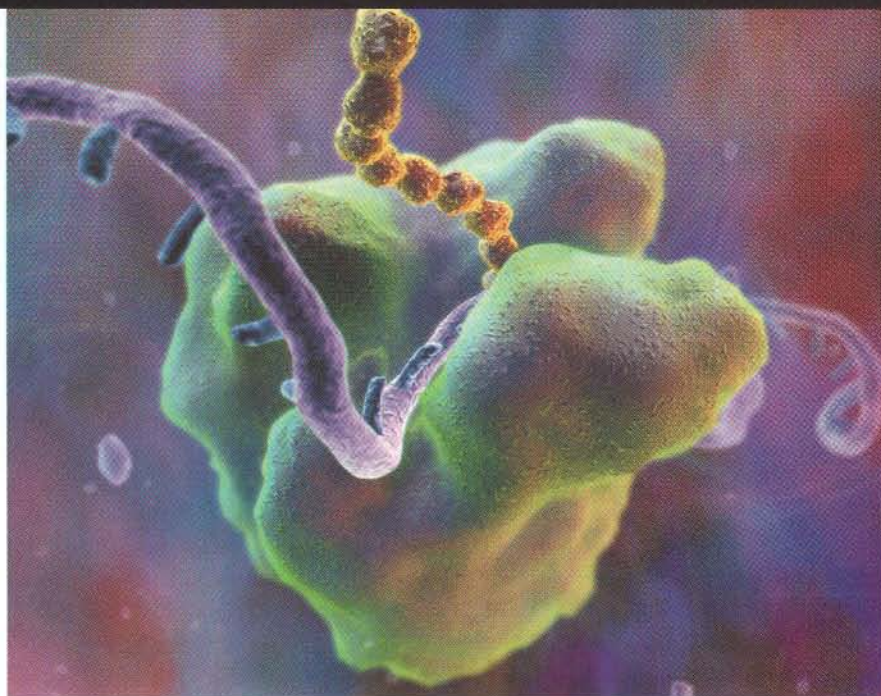
First is the pincers, or jaws, of the assembler. If they are to pick up atoms with any dexterity, they should be smaller than the atoms. But the jaws must be built of atoms and are thus larger than the atom they must pick and place. (Imagine trying to build a fine watch with your fingers, unaided by tools.) Second is the nature of atoms. Atoms, especially carbon atoms, bond strongly to their neighbors. Substantial energy would be needed to pull an atom from its place (a problem for the energy supply) and substantial energy released when it is put in place (a problem of cooling). More important, a carbon atom forms bonds with almost everything. It is difficult to imagine how the jaws of the assembler would be built so that, in pulling the atoms away from their starting material, they would not stick. (Imagine trying to build your watch with parts salvaged from another watch in which all the parts were coated with a particularly sticky glue: if you could separate the pieces at all, they would stick to your fingers.) Problems with the assembler are also discussed by Richard E. Smalley in his essay on page 68.

Would a nanosubmarine work if it could be built? A human-scale submarine moves easily in water by a combination of a rotating propeller—which, in spinning, forces the water backward and the submarine forward—and movable planes that guide its direction. Bacteria that swim actually use structures—fla-

gella—that look more like flexible spirals or whips but serve a function similar to a propeller. They typically do not steer a very purposeful path but rather dash about, with motion that, if all goes well, tends in the general direction of a source of food. For nanoscale objects, even if one could fabricate a propeller, a new and serious problem would emerge: random battering by water molecules.

These water molecules would be smaller than a nanosubmarine but not much smaller, and their thermal motion is rapid on the nanoscale. Collisions with them make a nanoscale object bounce about rapidly (a process called Brownian motion) but in random directions: any effort to steer a purposeful course would be frustrated by the relentless collisions with rapidly moving water molecules. Navigators on the nanoscale would have to accommodate to the Brownian storms that would crash against their hulls. For ships of approximately 100 nanometers in scale, the destination of most voyages would be left to chance, because the tiny craft would probably be impossible to steer, at least in a sense familiar to a submariner. Cells in the bloodstream—objects 10 or 100 times more massive than a nanosubmarine—do not guide themselves in it: they simply tumble along with it. At best, a nanosubmarine might hope to select a general direction but not a specific destination. Regardless of whether one could make or steer devices at the nanoscale, they would not work for the sophisticated tasks required to detect disease if one *could* make them.

Parts of the “little submarine” strategy for detecting and destroying diseased cells in the body, such as cancer cells, would have to focus on finding their prey. In doing so, they would probably have to mimic aspects of the immune system now functioning in us. The recognition of a cell as “normal” or “pathogen” or “cancer” is an extraordinarily complex process—one that requires the full panoply of our immune system, including the many billions of specialized cells that constitute it. No simple markers on the outside of most cancer cells flag them as dangerous. In many of their charac-



RIBOSOME reads along a strand of RNA (purple) to get instructions for stringing together the amino acids that constitute a protein (gold). This assembly-line process brings to mind the robotic welders in an automotive factory (opposite page).

teristics, they are not enormously different from normal cells. A little submarine that was to be a hunter-killer for cancer cells would have to carry on board a little diagnostic laboratory, and because that laboratory would require sampling devices and reagents and reaction chambers and analytical devices, it would cease to be little. Operating this device would also require energy. The cells of the immune system use the same nutrients as do other cells; a little submarine would probably have to do the same.

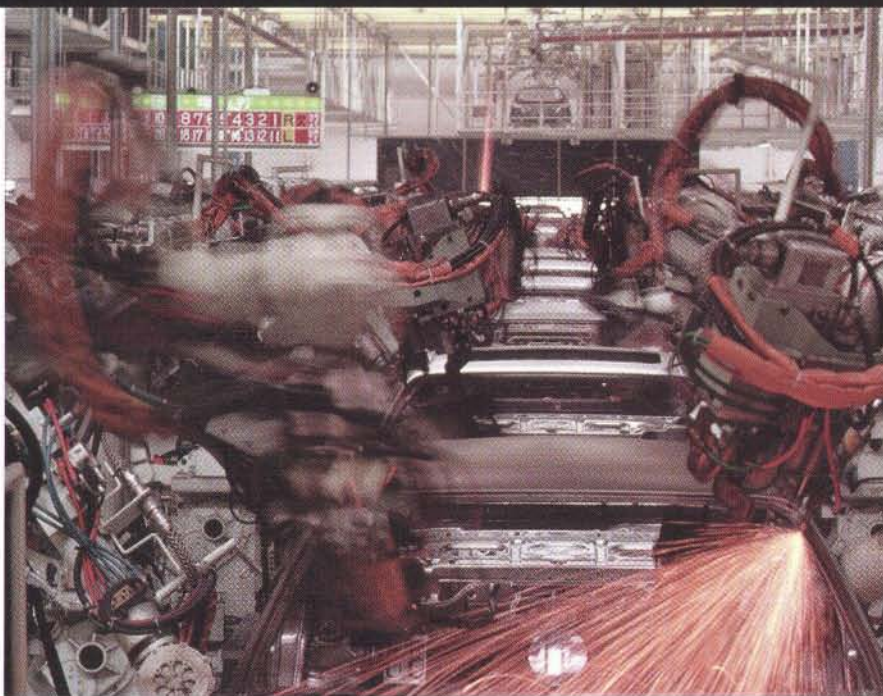
Outdesigning Evolution

SMALL MACHINES will eventually be made, but the strategy used to make them, and the purposes they will serve, remain to be devised. Biology provides one brilliantly developed set of examples: in living systems, nanomachines do exist, and they do perform extraordinarily sophisticated functions. What is striking is how different the strategies used in these nanometer-scale machines are from those used in human-scale machines.

In thinking about how best to make nanomachines, we come up against two limiting strategies. The first is to take existing nanomachines—those present in the cell—and learn from them. We will

undoubtedly be able to extract from these systems concepts and principles that will enable us to make variants of them that will serve our purposes, and others that will have entirely new functions. Genetic engineering is already proceeding down this path, and the development of new types of chemistry may enable us to use biological principles in molecular systems that are not proteins and nucleic acids.

The second is to start from scratch and independently to develop fundamental new types of nanosystems. Biology has produced one practical means for fabrication and synthesis of functional nanomachines, and there is no reason to believe that there cannot be others. But this path will be arduous. Looking at the machines that surround us and expecting to be able to build nanoscale versions of them using processes analogous to those employed on a large scale will usually not be practical and in many cases impossible. Machining and welding do not have counterparts at nanometer sizes. Nor do processes such as moving in a straight line through a fluid or generating magnetic fields with electromagnets. Techniques devised to manufacture electronic devices will certainly



be able to make some simple types of mechanical nanodevices, but they will be limited in what they can do.

The dream of the assembler holds seductive charm in that it appears to circumvent these myriad difficulties. This charm is illusory: it is more appealing as metaphor than as reality, and less the solution of a problem than the hope for a miracle. Considering the many constraints on the construction and operation of nanomachines, it seems that new systems for building them might ultimately look

ticular reaction catalyzed by this enzyme could be better. For most enzymes, and all structures more complicated than enzymes, we have made no effort to discover the alternatives.

Biological structures work in water, and most work only in a narrow range of temperatures and concentrations of salts. They do not, in general, conduct electricity well (although some, such as the chloroplast and the mitochondrion, move electrons around with great sophistication). They do not carry out bi-

fabrication. It must also be able to manufacture and assemble (or allow to assemble) all the pieces needed to make a copy of itself. Biology has solved all these problems, and self-replicating biological systems—from pathogenic bacteria to cancer cells—are a danger to us. In computer systems, self-replicating strings of bits (computer viruses), although not material objects, are also at least a great nuisance, but only indirectly a danger, to us.

If a new system—any system—were able to replicate itself using materials present in the environment, it would be cause for concern. But we now know enough to realize how far we are from reproducing self-replication in a nonbiological system. Fabrication based on the assembler is not, in my opinion, a workable strategy and thus *not* a concern. For the foreseeable future, we have nothing to fear from gray goo. If robust self-replicating micro (or perhaps nano) structures were ultimately to emerge, they would probably be chemical systems as complex as primitive bacteria. Any such system would be both an incredible accomplishment and a cause for careful assessment. Any threat will not be from assemblers gone amok but from currently unimaginable systems of self-catalyzing reactions.

So biology and chemistry, not a me-

It will be a marvelous challenge
to see if we can outdesign evolution. It would be a staggering
accomplishment to mimic the simplest living cell.

much like the ancient systems of biology. It will be a marvelous challenge to see if we can outdesign evolution. It would be a staggering accomplishment to mimic the simplest living cell.

Are biological nanomachines, then, the end of the line? Are they the most highly optimized structures that can exist, and has evolution sorted through all possibilities to arrive at the best one? We have no general answer to this question. Jeremy R. Knowles of Harvard University has established that one enzyme—triose phosphate isomerase, or TIM—is “perfect”: that is, no catalyst for the par-

nary computation and communications. They are not particularly robust mechanically. Thus, a great many types of function must be invented if nanomachines are to succeed in nonbiological environments.

And what have we learned from all this about the doomsday scenario of gray goo? If a hazard were to arise from nanomachines, it would lie in a capability for self-replication. To be self-replicating, a system must contain all the information it needs to make itself and must be able to collect from its environment all the materials necessary both for energy and for

mechanical engineering textbook, point in the direction we should look for answers—and it is also where our fears about organisms or devices that multiply uncontrollably are most justified. In thinking about self-replication, and about the characteristics of systems that make them “alive,” one should start with biology, which offers a cornucopia of designs and strategies that have been successful at the highest levels of sophistication. In tackling a difficult subject, it is sensible to start by studying at the feet of an accomplished master. Even if they are flagella, not feet.

■

| By Steven Ashley

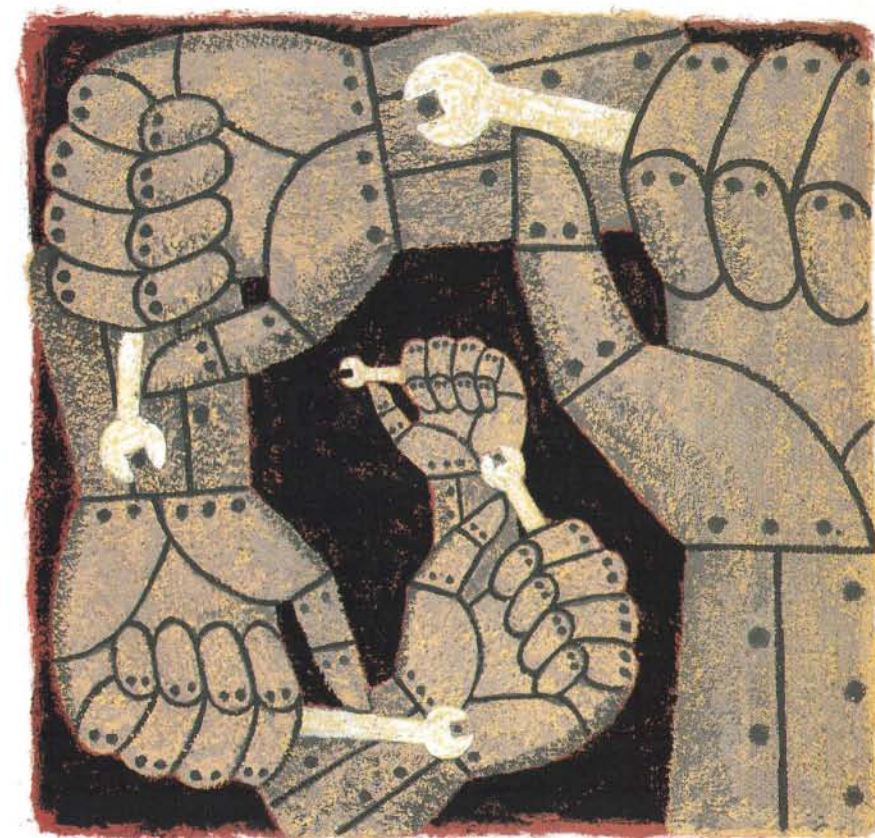
Nanobot Construction Crews

Nanotechnology visionaries find out how difficult it is to develop minuscule robots that can treat diseases or perform pollution-free manufacturing

MOLECULAR MANUFACTURING—the heady notion of assembling almost anything, from computers to caviar, from individual molecules—would change the world, if someone could just find a way to make it work. Imagine nanoassemblers: busy work gangs of “pick and place” robotic manipulator arms, each one tens of nanometers in size. Controlled from on high by a powerful computer, these simple devices would arrange blocks of molecules to make copies of themselves—and these machines would, in turn, build still other nanomachines, which, in turn, would create others, and so on in an exponential expansion. These nanobot construction crews could then be directed to accomplish astonishing tasks such as curing diseases from inside the body and fabricating intricately engineered materials from basic bulk feedstocks at extraordinarily low cost.

For years, futurist K. Eric Drexler and his colleague Ralph C. Merkle, the noted cryptographer, nurtured this vision, using computer simulations of nanometer-scale gears, pumps and other molecular machine subsystems. In these images, colored spheres indicate the position of each component atom. Several analytical critiques of these elaborate simulations suggested that the devices simply wouldn’t work as hoped. But perhaps the most biting criticism focused on their status as mere digital representations and not real-world objects interacting with complex chemical bonding forces in the nanoscale environment, where macroscale physics doesn’t always apply and quantum mechanics often prevails.

Then, in 1999, Merkle decided to leave a long-term position at the Xerox Palo Alto Research Center to try to give



real substance to his computer-concocted concepts. He joined software mogul James R. Von Ehr II, an admirer of Drexler’s ideas, who had decided to spend part of the “low-nine-figure” fortune he garnered from the sale of his company, Altsys, to start the first “molecular nanotechnology” company.

Zyvox, the Richardson, Tex.-based company Von Ehr founded, is aiming high. “We’d love to be the Applied Materials for the manufacturing base of the world,” he says, referring to the world’s leading semiconductor equipment manufacturer. But his molecular nanotechnology company is still in the early stages

TOP-DOWN FABRICATION is one pathway Zyvox is taking toward molecular manufacturing.

of its quest. Its experience has already demonstrated the difficulty of moving from software-wrought molecular machines to a real-world nanoassembler. One of the first things the company had to do was to pull back from the idea of building things atom by atom. Today the long-term focus is on fabricating nanoscale machine systems from large molecules or blocks of molecules. To that end, company scientists are experimenting with the bottom-up approach to making assemblers with molecular nanotechnol-

ogy—learning to put together structures molecule by molecule using atomic force microscopes and the like.

In the near term, Zyvex researchers are developing microelectromechanical systems (MEMS), whose structures measure in tens of microns. MEMS devices are manufactured using a top-down approach. They are lithographically patterned and etched out from silicon substrates or other materials.

Richard Feynman, the ur-guru of the field, did say that bigger machines could be used to make smaller machines. And that's where MEMS comes in. According to Merkle, MEMS fabrication methods can be used to build robotic assembly arms. These microelectromechanical "hands" can assemble submicron hands that can build even tinier hands, and so forth, step by step until the ultimate in mechanical smallness is achieved: the nanoassembler, a nanometer-scale manufacturing device. For Zyvex to accomplish its goal, the MEMS robots that it creates must be shrunk by a factor of 1,000 or so. Once the requisite downsizing has been completed, nanobots, as envisaged, will be used for "atomically precise manufacturing" to make virtually anything. Universal constructors could manufacture a Rolex watch, followed by a computer memory and then by nanomachines that can treat diseases.

Two basic ideas underlie Zyvex's road to nanorobotics, Merkle says. In positional assembly, mechanical manipulators pick up and precisely place objects into assemblies. Accurate positional control at scales of tens of nanometers means moving large molecules or blocks of molecules where you want them and causing them to bond to an assembly as desired.

A machine that can build a complex material or device from the bottom up—using an Erector set of molecules or chunks of molecules for components—will require one other critical technology: the machine must be able to make a copy of itself. "If you wish to achieve economical production of molecular devices in large numbers, some form of self-replication is necessary," Merkle explains. And unless you had hordes of nano-

constructors on the job, building macro-scale objects molecule by molecule would take a very long time. Zyvex researchers note that a fully self-replicating machine would not be necessary to manufacture an assembler. Still, the task is a monumental one: any machine outside the biological sphere that could make any number of copies of itself would probably lead to a Nobel Prize, possibly several.

So how does Zyvex get to an assembler? Recently Zyvex joined with Standard MEMS in Burlington, Mass.—a company that fabricates microsystems—in a two-year collaborative program to develop lithographically formed micron-scale manipulator arms and grippers that can assemble smaller manufacturing devices from pallets of precisely positioned "active" parts produced on silicon wafers. "If the positional accuracy is good enough, the arm simply has to reach down and pick the part up. You don't need an elaborate sensing system," Merkle says.

According to Von Ehr, Zyvex researchers have developed a method by which the MEMS manipulator can detach the parts from the substrate so they are ready for microassembly using self-centering snap-connectors—a useful, if not exactly new, capability. Manipulator parts would be created lithographically, etched out and then disconnected from the surface substrate so they could be picked up by the MEMS manipulator and attached to the device by snapping them into place. Von Ehr hopes these MEMS manipulators will prove to be an intermediate technology that could serve as a moneymaking product, such as a device to align a fiber-optic cable, as the company pursues its goals.

Unfortunately, it's hard to find anyone in the MEMS field who would be interested in this kind of technology or anyone who can contemplate what kind of product it would actually be used to build, says Kaigham J. Gabriel, now professor of electrical and computer engineering and robotics at Carnegie Mellon University and former director of the

MEMS program at the Defense Advanced Research Projects Agency.

And what about the nanoscale assembler? "There is significant controversy about how long it will take to achieve ultimate control at the molecular level," Merkle notes, adding that "it could take a decade or two."

So Zyvex has its work cut out for it.

But it has embarked on a mission to achieve the nanoequivalent of a moon shot in relative isolation with a staff of only 37. In general, the scientific research community has distanced itself from this project. Several scientists

working in the field of nanotechnology derided Zyvex's scheme but requested anonymity to avoid protests from amateur nanotech enthusiasts. Says one researcher, "We've seen no experimental proof that any portion of their scheme can actually be accomplished. We think it's a lot of nonsense." Merkle responds that "nothing we propose contradicts the laws of physics."

Meanwhile, with Von Ehr's fortune backing up the research effort, Zyvex can continue to function for many years without having to market a product, but the entrepreneur allows that it would be nice to make some money. "This whole thing is a lot harder than it first seemed," he admits. Von Ehr has reportedly already spent about \$20 million on the project, but considering last year's stock market fall and the reality of the task looming on the horizon, he says he is planning to seek outside investment once financial conditions improve. "If we're going to grow," he says, "we'll need more money."

No matter how big the envisioned payoff, however, given the daunting technical difficulties and a 10- to 20-year timeline to possible success, one wonders just who would be willing to put up significant investment funds. Perhaps Zyvex's trek toward molecular nanotech could be financed by small contributions from its legions of true believers. ■

Steven Ashley is a staff editor and writer.



| By Graham P. Collins

Shamans of Small

Like interstellar travel, time machines and cyberspace, nanotechnology has become one of the core plot devices on which science-fiction writers draw

"READING DREXLER'S *Engines of Creation* in 1990 went into the making of the world in *Queen City Jazz*, my first novel, though the book drew from many other sources: Shakers, ragtime, jazz, American literature, even Krazy Kat." So writes Kathleen Ann Goonan in the Summer 2001 *SFWA Bulletin*, the quarterly of the Science Fiction and Fantasy Writers of America, in a brief essay about her award-nominated novel *Crescent City Rhapsody*, the third book of her musically structured Nanotech Quartet.

Unsurprisingly, Goonan is far from the only science-fiction writer to take inspiration from K. Eric Drexler's vision of molecular nanotechnology, for it is a vision that connects to numerous preexisting themes of science fiction and offers writers an extraordinarily broad palette of capabilities, all imbued with the appearance of scientific plausibility. Tout-

ed by its proponents to be upon us within a decade or few, nanotechnology also gives science-fiction writers a chance to engage in the art of predicting and warning about possible futures. This role as an ad hoc think tank is one that innumerable science-fiction writers and fans take on enthusiastically, not only in their fiction but also in endless earnest panel discussions at conventions, in online newsgroups and discussion boards, and in articles labeled (sometimes optimistically) nonfiction. It is the culture of the intensely technophilic—even those who write of techno-dystopias and apocalypses are enrapt in a love-hate relationship with science and technology. The borders between four dominions—those of scientists, writers, readers and science-fiction fans—are hopelessly blurred, with countless individuals holding joint citizenships.

But it would be a mistake to think that science fiction's central role is one of serious prognostication. The question "What if...?" lies at the heart of science fiction, but what comes after the ellipsis and the answers that stories give are ultimately not science but literature—that strange mix of entertainment and meaningful enrichment of life. The art of any fiction writer is the art of the storyteller. As Kathryn Cramer (writer and anthologist and daughter of physicist and fiction writer John G. Cramer) writes in *The Ascent of Wonder*:

The majority of science fiction stories are not plausible extrapolations upon our current situation, using available information; rather they are Escheresque impossible objects which use the principles of science in much the same way

that Escher used rules of geometric symmetry—the rules give form to the impossible imaginative content.

Antediluvian Nanotech

MANY OF DREXLER'S imaginings have antecedents in science fiction and feed into old potent themes of the genre. Science fiction has long been fascinated with machines in general, such as in the stories of Jules Verne. The absolute control of matter promised by nanomachines is a variant of the dream that *Homo sapiens* can achieve complete mastery over nature and has utter freedom to shape its own destiny. The dark vision of nanobots running amok is a new wrinkle on the old golem/Frankenstein myth, the dangers of meddling with godlike powers or bringing too much hubris to science. The bright vision of the world, and indeed the nature of humanity, being transformed into something transcendent and new is another science-fiction standby.

Nanotech burst into the collective consciousness of technology aficionados at a good time to interface neatly with the mid-1980s wave of cyberpunk stories, in which characters experience the completely programmable virtual realities of cyberspace. With full-scale molecular nanotech it is not just *virtual* reality that is programmable. The intelligent agents and viruses of cyberspace become free to roam about in the air that we breathe and within our bodies—a curious inversion of people loading their consciousnesses into machines.

MICROSCOPIC CRAFT, built using nanotech, battle foreign invaders the way an immune system does. Even the implant-enhanced eye sees only a fog sparkling with laser light.

NANOTITLES DISCUSSED

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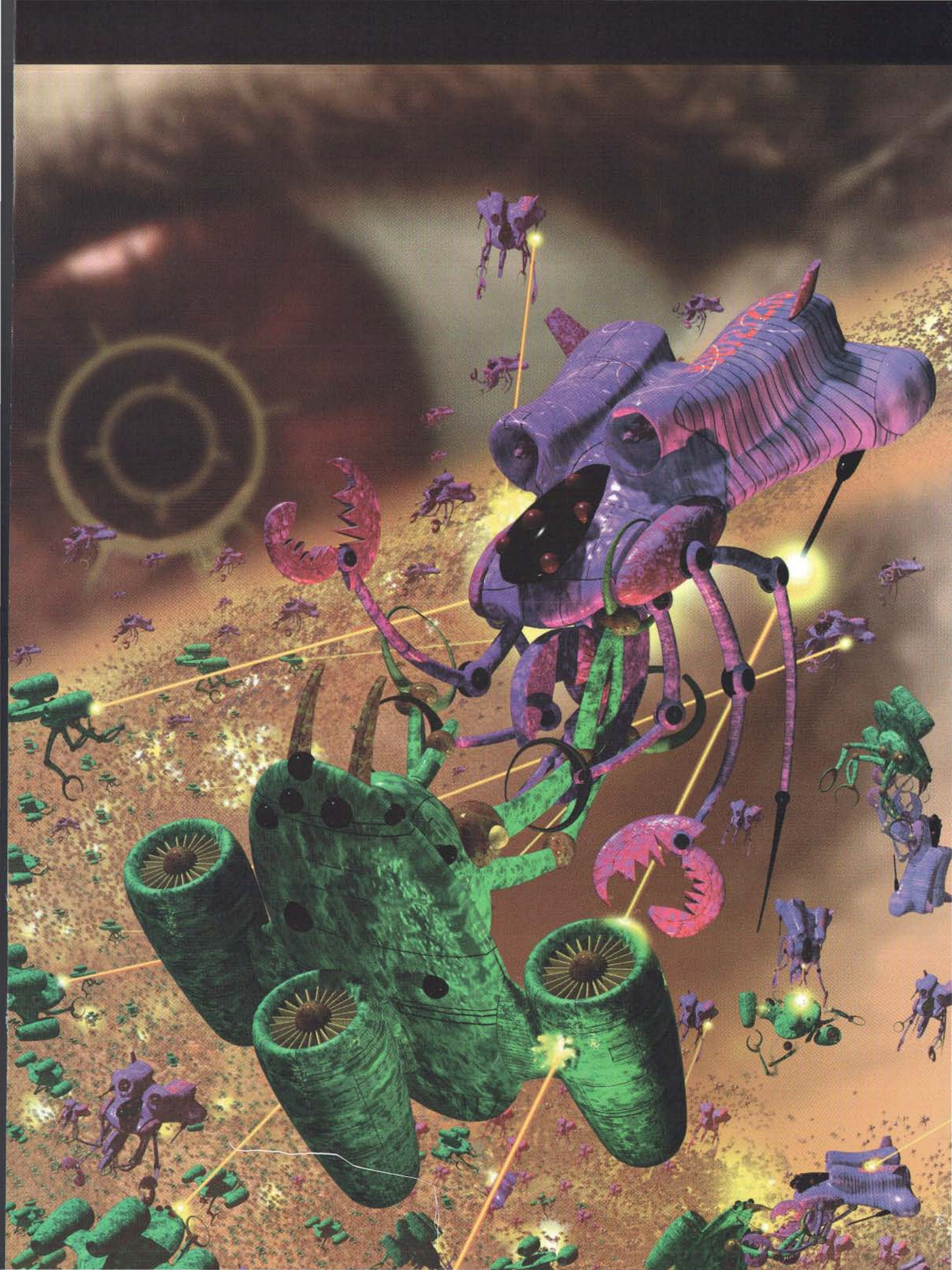
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The prospect of absolute control of matter using nanomachines

is a variant of the dream that *Homo sapiens* can achieve complete mastery over nature.

Elements suggestive of now common nanotech themes appeared in science fiction well before the advent of the term "nanotech." The concept of microscopic surgery appeared in the 1966 movie *Fantastic Voyage*, novelized by Isaac Asimov. Of course, instead of using molecular machinery built of real atoms, a large scientific-looking contraption magically reduces people and machinery to microscopic scale by shrinking their very atoms, in violation of numerous physical principles. Interestingly, the 2001 novel *Fantastic Voyage: Microcosm*, by Kevin J. Anderson, uses the miniaturization technology of *Fantastic Voyage* to ex-

plore the dormant body of an alien from a shot-down UFO. Lo and behold, the Lilliputian explorers find themselves confronting alien nanotechnology.

Progenitors of nanotech fiction extend back even further. In the classic 1941 story by Theodore Sturgeon, "Microcosmic God," a scientist creates a society of miniature creatures ("Neoterics") that evolve at a rapid pace and produce technological wonders. This theme is picked up in a modern way in *Blood Music*, by Greg Bear, first published as a novelette in the magazine *Analog* in 1983 and expanded into a novel in 1985. Despite predating the popularization of nanotech, *Blood Music* is frequently cited as a seminal nanotech story and included in nanotech anthologies. In the story, a researcher creates intelligent cells, "nocytes," that escape from confinement and spread like an epidemic through humanity, destroying it but also seemingly bringing about a transcendental change to a new form of existence. It's the end of the world as we know it, but we'll all feel fine afterward.

Television has also picked up on Sturgeon's concept. In the 1996 Halloween episode of *The Simpsons*, Lisa accidentally creates a microscopic society (ingredients: a tooth, Coca-Cola and an electric shock delivered by Bart) that rapidly advances from the Stone Age through the Renaissance and then far beyond our own technology. The theme is combined more soberly with the modern concept of nanotech in the episode "Evolution" of *Star Trek: The Next Generation*, which aired in 1989, just three years after Drexler's *Engines of Creation* hit the bookstores. Boy wonder Wesley Crusher accidentally releases some "nanites," tiny robots designed to work in living cells, which proceed to evolve into a highly intelligent society that invisibly infests the systems of the starship *Enterprise* and starts wreaking havoc. Fortunately, in classic *Next Generation* style, at the last minute, contact is made with the evolved

nanites, and a mutually acceptable peaceful outcome is negotiated: they are placed on a convenient planet where they'll have more room to live and grow. If only every conflict, plague or technological disaster in the real world were solvable with such ease and rationality.

The central feature of molecular nanotechnology, precise manipulation of atoms, crops up in a classic science fantasy of 1965:

The stuff was dancing particles within her[....] She began recognizing familiar structures, atomic linkages: a carbon atom here, helical wavering ... a glucose molecule. An entire chain of molecules confronted her and she recognized a protein ... a methyl-protein configuration.

[...] she moved into it, shifted an oxygen mote, allowed another carbon mote to link, reattached a linkage of oxygen ... hydrogen.

The change spread ... faster and faster as the catalysed reaction opened its surface of contact.

The novel? *Dune*, by Frank Herbert, in which computers are banned throughout the empire and spaceship pilots navigate through hyperspace by means of drug-induced precognition. While Paul Atreides is on his way to becoming the messianic ruler of the known universe, his mother, Lady Jessica, takes part in a ritual involving "the water of life"—a deadly poison related to the "melange," or "spice," that feeds supernatural powers of intuition and prescience. To survive the ritual, Jessica's consciousness dives down into inner space and slows time to a crawl to analyze the chemical composition of the poison on her tongue and, using a "psychokinesthetic extension of herself," transform it into a catalyst that rapidly detoxifies all the rest of the poison, turning it into a potent but not deadly narcotic.

Yet except for the use of psychoki-

STORY EXCERPT:


EVERYDAY NANO-NOVELTIES

WE WERE OUT OF OUR MINDS WITH JOY,
BY DAVID MARUSEK (from Asimov's *Science Fiction*, November 1995)

I held patents for package applications in many fields, from emergency blankets and temporary skin, to military camouflage and video paint. But my own favorites, and probably the public's as well, were my novelty gift wraps. My first was a video wrapping paper that displayed the faces of loved ones (or celebrities if you had no loved ones) singing "Happy Birthday" to the music of the New York Pops. That dated back to 2025 when I was a molecular engineering student.

My first professional design was the old box-in-a-box routine, only my boxes didn't get smaller as you opened them, but larger, and in fact could fill the whole room until you chanced upon one of the secret commands, which were any variation of "stop" (whoa, enough, cut it out, etc.) or "help" (save me, I'm suffocating, get this thing off me, etc.).

Next came wrapping paper that screamed when you tore or cut it. That led to paper that resembled human skin. It molded itself perfectly and seamlessly (except for a belly button) around the gift and had a shelf life of fourteen days. You had to cut it to open the gift, and of course it bled. We sold mountains of that stuff.



INVISIBLE NANOTECH pervades this scene from Greg Bear's novel / *[Slant]*. Mary Choy has transformed her features back to her original Asian look. The pyramidal building is reinforced with flexfuller and contains cryopreserved bodies of the rich and privileged. The swanjet has no conventional ailerons; instead nanodevices on each wing surface control the lift forces by forming thousands of tiny vanes or humps.

nesis in place of a technological framework, the entire process sounds like a nanotech engineer working at a virtual-reality station to design a molecule. Or like a scenario from *Unbounding the Future: The Nanotechnology Revolution*, by Drexler, Chris Peterson and Gayle Pergamit, in which a tourist experiences a museum exhibit that simulates the molecular-scale world, complete with scaling (slowing down) of time. In essence, nanotechnology offers to make *Dune*'s fantasy of complete human control over the self and the rest of the universe into a reality but in a mass-produced industrial fashion rather than through intensive individual training and drug-enhanced psychic powers.

Nanotech is also prefigured in *Dune* through the Ixians, traders from a rare high-tech corner of the universe who are "supreme in machine culture. Noted for

miniaturization." Indeed, devices from *Dune* such as the "hunter-seeker," a tiny poison-tipped flying needle, would be completely at home in nanotech stories.

Hot Stuff

NANOTECHNOLOGY'S use in science fiction takes many forms, classifiable by a number of measures. The role of nanotech ranges from a central part of the plot to a relatively incidental part of the fictional world. The nanotech may be developed by humans, or it may be a gift from aliens, or it may *be* the aliens. The technology may work according to well-defined rules, or it may be arbitrary magic, scantily clad in trappings of science. The rules may be expressly mentioned in the text (perhaps even laboriously described), or the work may rely on the reader to tap into a science-fictional consensus reality, acquired from reading ear-

lier stories, of what generic Acme nanotech can and can't do.

Both of the latter alternatives relate to two approaches to presenting technology in science fiction. At one extreme, the text practically contains a research paper on the author's hyperspace theory and blueprints of the first starship (rather like some of the letters *Scientific American* receives). At the other, famously pioneered by Robert A. Heinlein, the technology is dropped in without explanation: "The door dilated." In three words we know we are in a future with strange new technologies, and we are really *there* because in the future commonplace devices such as dilating doors need no more explanation than cellular phones do today.

When you read a large number of nanotechnology stories in a short space of time, some amusing recurring themes



MINIATURIZED PEOPLE in the 1966 movie *Fantastic Voyage* swim like nanobot surgeons in a patient's bloodstream.

appear. On the one hand, nanotechnology often becomes a means to accomplish anything within the realm of the imagination, while conveniently ignoring the constraints of physical laws. Curiously, on the other hand, these stories reveal some of the actual technical challenges that molecular nanotechnologists might confront if they ever were to execute their designs for real-world nanobots. For example, it seems that most everyone writing nanotech fiction is aware that highly active nanocritters will generate heat, a problem of some concern when said nanocritters are functioning inside your body.

In one of the early stories, the 1989 novella *Nanoware Time*, by Ian Watson, the nanoware has been brought to humankind by seemingly benevolent aliens that look like giant golden centipedes. When the nanoware is injected into a person, it takes root in the subject's brain, supplying him or her with the power to ... (can you guess?) harness "demons" from a parallel dimension. These demons have no will of their own but possess extraordinary powers that the nanowired person can then use, for

instance, to shield himself from the vacuum of space, propel a starship across the galaxy, fire bolts of energy for good or ill, and so on. The nanoware is really just a technological cloak for supernatural magic. In another era the alien device would have been some other mind-enhancing black box or injectable drug. Yet because this is nanoware—nanobots that rewire the hardware and software of your "wetware" (your brain)—one does have to worry about the heat generated by its functioning. A few of the early human volunteers fried their brains before the right parameters for humans were worked out:

Heat was a byproduct of all the rapid molecular activity in the skull while the busy little nanomachines built the nanoware. Thus some brains got cooked.

Vance was among the survivors. [His] brain damage was repaired by other nanos; sort of repaired. He'd been rehabilitated, retrained as a waste recycler.

In one of the many plot threads in the 1997 novel */[Slant]*, by Greg Bear,

a sequel to the landmark *Queen of Angels* (1990), four people are found dead in an illicit body-modification clinic: they were cooked, literally, when the body-modifying nanotech ran amok. The cause is promptly uncovered by investigators when they examine the jars of pastelike "nano" on the shelf:

Mary picks up a bottle, reverses it to read the label.[...] The label confirms her suspicions.[...]

"This isn't medical grade," Mary says. "It's for gardens.[...] Any real expert could reprogram it. Apparently they didn't have a real expert."

Presumably the victims were broiled because a bug in the badly reprogrammed garden-grade nano made it run wild, generating far too much heat in the process.

Later in the book a group of criminals who have infiltrated a huge tetrahedral building make use of some illicitly obtained MGN—military-grade nano. Sprayed from a canister like fire-extinguisher foam, the nano deconstructs objects present in the building's garage and rebuilds the atoms into intelligent robotic weaponry. During this process the garage heats up like an oven, but not too hot, because "at about four hundred degrees, nano cooks itself."

A spectacular case of spontaneous human nanocombustion occurs in one of the most surreal sections of Neal Stephenson's tour de force *The Diamond Age*. A secluded cult known as the Drummers is infected with millions of nanoprocessors. When two processors meet in someone's bloodstream, they compare notes, perform a computation and then go on their way: a kind of distributed, Internet-like supercomputer. The computation proceeds mostly at a steady pace, but occasionally it advances in a spurt of activity when myriad parallel threads of the computation are brought together for synthesis by an orgy (exchange of bodily fluids is the key means of transferring these processors and their data between people). The orgy culminates when the nanoprocessors are loaded into one unlucky woman who is promptly incinerated by the heat

Anyone can obtain free food from public nanotech matter compilers, but they're not up to the cordon bleu standards of *Star Trek's* replicators.

of the nano-orgy that ensues in her bloodstream. To access the computation's result, the other Drummers mix her ashes into a soup—highly reminiscent of the Martian process of “grokking” the dead (in essence, ritual cannibalism to honor and fully appreciate the deceased) in Robert A. Heinlein's 1961 novel *Stranger in a Strange Land*, but with the patina of a scientific rationale.

Stephenson's *The Diamond Age* and

STORY EXCERPT: DYSTOPIAN NANO-FUTURE

NO LOVE IN ALL OF DWINGELOO, BY TONY DANIEL (from *Asimov's Science Fiction*, November 1995)

[We lived] on Kokopelli Station. There were more people living up-cable, thousands and thousands more. Still, this was just a trickle of refugees compared with the billions who had died below. Earth was horribly worse, and it was then that I realized I was seeing the future.

The squabbles and wars of the present had played themselves out and we'd done it, we'd ruined the planet. The seas were biohazard cauldrons, seething with an ecology of war viruses. The land was haunted by nanoplasm, the primal form that life had taken, been reduced to. Sea and land were at war—over nothing, any longer—just a meaningless perpetual struggle between viral life and nano algorithms caught in a perpetual loop. Those who crafted the weaponry were dead.

A few million humans survived on the coasts, in the land between the warring elements. They were temporarily immune to the nano, but none could say for how long, since the nano evolved, its sole purpose finding ways to beat back the living, zombie sea—and, incidentally, to remake whatever people remained into a substance that could not wield a gun and could not think to use one.

Yet I found myself completely, unshakably content. Kokopelli was safe. We had severed all but one cablelift, and created defenses that kept the muck below at bay.

Bear's *Queen of Angels* are comprehensive depictions of societies completely changed by nanotechnology. In *Queen of Angels*, a large proportion of the populace has been “therapied,” in which injected nanotech devices infiltrate a person's brain to correct psychological imbalances and weaknesses. Many people undergo extensive nano-enabled body modification, ranging from practical enhancements for their occupation to beautification and the addition of exotic features. A complex tension runs through the society because of prejudices and attitudes about “transforms,” “high naturals,” and “therapied” and “simple untherapied” individuals.

In Bear's world, nano comes in jars like paste. In Stephenson's *The Diamond Age*, the key to nano is “the feed,” a type of nanopipeline that runs into every household, supplying atoms as needed by matter compilers, which are as common as microwave ovens are today. Anyone can obtain free food from public matter compilers, but they're not up to the cordon bleu standards of *Star Trek's* replicators; rice they can do, but green vegetables come out as a paste. Airborne nanotech is ubiquitous, ranging from almond-size surveillance monitors to microscopic attack and defense craft engaged in a constant struggle, like an immune system battling invaders. On bad days in the poor section of town, this ongoing contest looks like a fog shot through with firefly sparkles of laser light. A sootlike coating composed of casualties from this conflict settles on everything and everyone. Wealthier enclaves, such as that of the Vickys (neo-Victorians), are protected from such troubles by a deep defensive perimeter of airborne nanobots.

Nanofiction is not without humor. *The Diamond Age*, particularly early in the book, is told with abundant wit and drollery. The story opens with the exploits of a spectacularly stupid lowlife named Bud. A parody of the Walkman

generation, Bud gets around on in-line skates capable of a top speed of more than 100 kilometers an hour, and his music system is “a phased acoustical array splayed across both eardrums like the seeds on a strawberry.” He's sometimes a little “hinky” on the skates: implanted nanosites incessantly twitch his muscle fibers to maximize their bulk. Together with a testosterone pump in his forearm, “it was like working out at a gym night and day, except you didn't have to actually do anything and you never got sweaty.”

And isn't that, in the end, what much of nanotech is about? A quasi-scientific way to get what you want effortlessly and at minimal cost. Instant gratification through the ultimate in high technology. Compile your dreams and gather a bunch of atoms. Just add nano.

Graham P. Collins is a staff editor and writer. He is also an occasional science-fiction writer and the webmaster of the *Science Fiction and Fantasy Writers of America*.

MORE TO EXPLORE

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Magazine of Fantasy & Science Fiction: www.sfsite.com/fsf/

Sci Fiction: www.scifi.com/scifiction/

WORKINGKNOWLEDGE

FLEA TREATMENTS

Killer Drops

Shampoos, powders, sprays and collars all aim to control fleas on pets, but the most popular treatments today are the "spot" medications. Squeeze a few drops on the skin along a dog's or cat's back, and the insecticide will control fleas for a month. The products are available only from veterinarians, in doses adjusted for an animal's weight.

The formulations spread by mixing with a pet's skin oils, which migrate as a result of body movement and gravity. Some products flow into the sebaceous glands of hair follicles, where they are stored and secreted over time; others remain on the skin's surface. Advantage (imidacloprid) from Bayer and Frontline (fipronil) from Merial—the two market leaders—will fan out across the body in less than 12 hours and kill more than 90 percent of fleas by then. Tests by Bayer show that after 28 days, concentrations across a dog's body decrease to as little as one part per million, but less than one tenth of that amount is needed to kill fleas, according to Bob Arther, Bayer's manager of parasitology. And because they reside in or on skin, spot compounds do not readily wash off like treatments that stick to an animal's hair.

Pets can be given anti-flea pills, sending medication into their bloodstream. But a flea must bite the pet to be exposed to the insecticide. Some pills do not kill adult fleas but make their eggs unviable. The spot treatments kill virtually all fleas within 18 hours and prevent eggs from being laid. Buyers should be wary of over-the-counter knockoffs; many contain permethrin, which is less effective on dogs and is toxic to cats.

Some critics claim that pets can be harmed by ingesting small amounts of spot treatments as they groom themselves (although the same could be said of a spray, collar or pill). But tests required by the Environmental Protection Agency show that "animals that had received even gross overdoses had no change in their kidney or liver values," says Bruce Klink, manager of veterinary services at Merial. Manufacturers say the active ingredients do not affect people.

No insecticide is 100 percent safe. But be skeptical about "natural" or "chemical-free" alternatives such as vitamin B or garlic. There is little scientific proof that the potions send fleas fleeing.

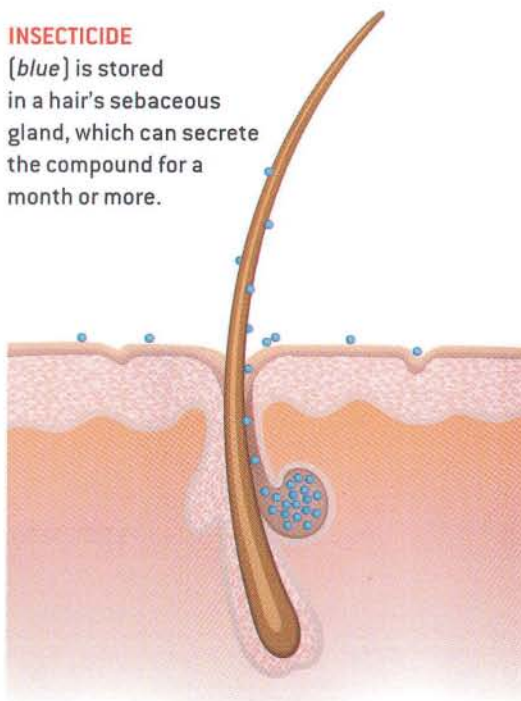
—Mark Fischetti

"SPOT" FLEA TREATMENTS

mix with a pet's skin oils. A few drops disperse readily. Tests by maker Merial on midsize dogs given the recommended dose of the treatment fipronil show that concentrations quickly spread across the body. And although concentrations are low after 56 days, they are still high enough to kill fleas [95 percent of fleas die when exposed to 0.7 microgram per gram of fur].

INSECTICIDE

(blue) is stored in a hair's sebaceous gland, which can secrete the compound for a month or more.



➤ **FADING FAD:** When a flea bites, it deposits saliva in the skin. Pets can have an allergic reaction that causes redness and severe itching. As they scratch, they develop flea-allergy dermatitis. For years, FAD was the leading skin problem in dogs and cats, but veterinarians report that "spot" treatments, because of their quick kills, have dramatically reduced the incidence of the disorder.

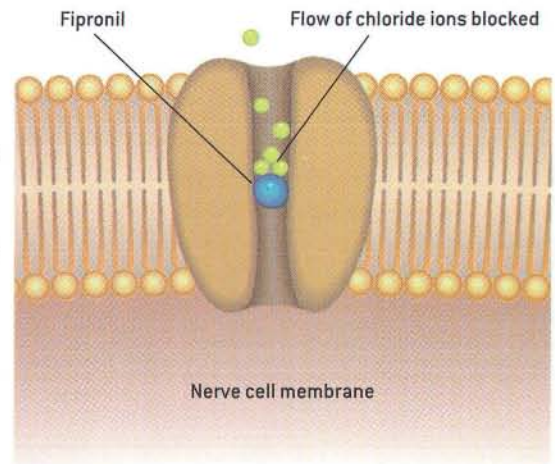
➤ **BLACK DEATH:** Rat fleas carry bacteria that can cause plague, such as the bubonic plague that wiped out one third of Europe's population in the 14th cen-

tury. In 1999 microbiologists identified plague in flea-infested squirrels, chipmunks and other wild rodents in 22 counties surrounding Sacramento, Calif.; in 2000 state health officials began issuing regular warnings about plague-prone areas there.

➤ **MAN BEFORE BEAST:** The French established the world's first veterinary school, in Lyon in 1762. Veterinary science was originally developed not so much to help animals but to improve the understanding of zoonotic diseases in order to prevent their transfer to humans.

FLEA'S NERVE CELL

is the target of the spot medication's active ingredient, which binds to a specific receptor there. The treatment fipronil (shown at right) blocks the flow of chloride ions that otherwise interrupts nerve signals. This hyperexcites a flea's central nervous system, sending it into a deadly seizure.

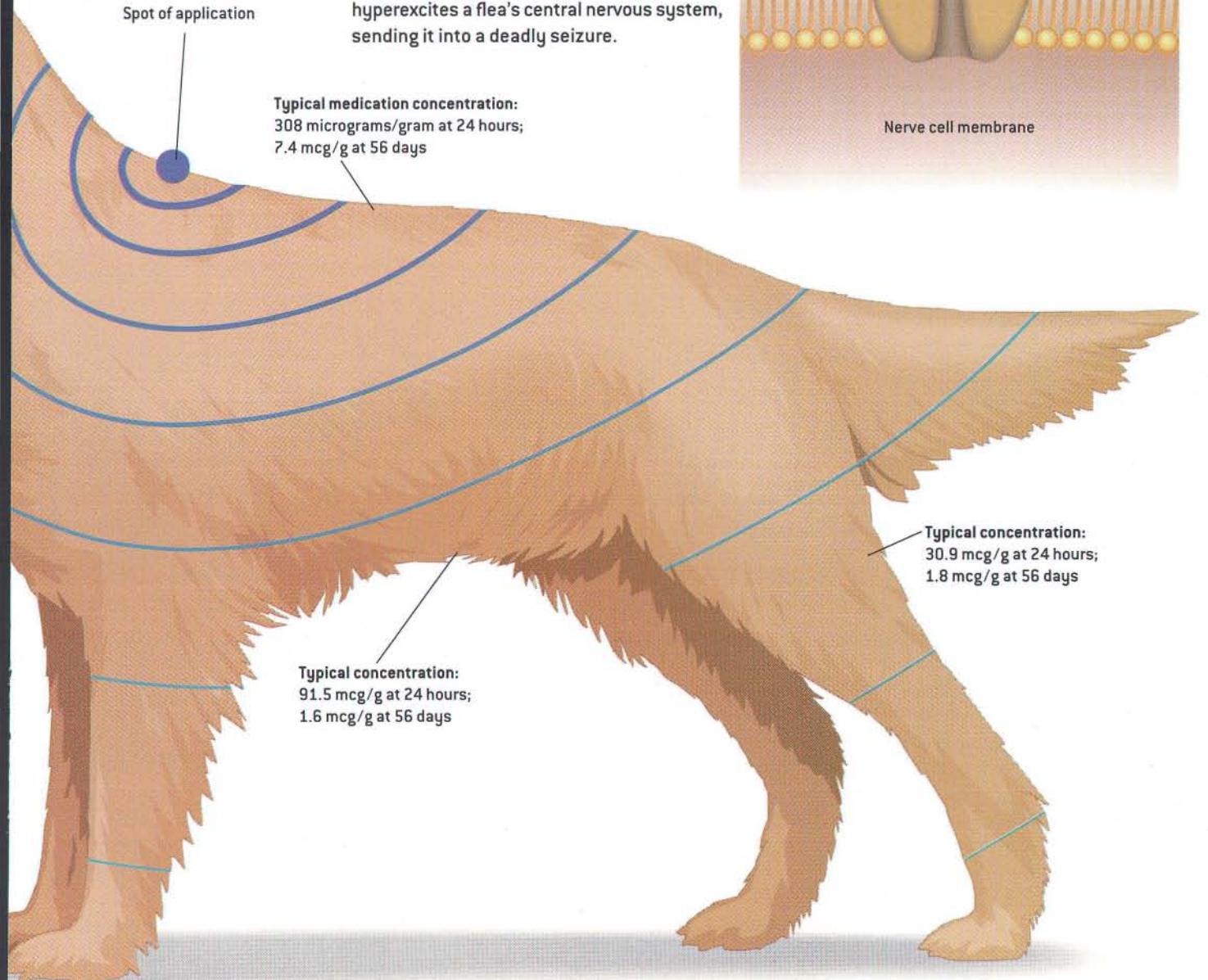


Spot of application

Typical medication concentration:
308 micrograms/gram at 24 hours;
7.4 mcg/g at 56 days

Typical concentration:
91.5 mcg/g at 24 hours;
1.6 mcg/g at 56 days

Typical concentration:
30.9 mcg/g at 24 hours;
1.8 mcg/g at 56 days



Seeing the Earth for Its Faults

GEOLOGICAL TOURS AND GUIDES EXPOSE THE SECRETS OF NEW YORK CITY AND BEYOND BY MARGUERITE HOLLOWAY

Continents collided—northwestern Africa crashed and ground against North America—and mountains as tall as the Alps rose in New England. Wind and rain beat at the peaks and wore them down, and then the land on which they stood sank below the sea. Waves and tides had their turn, and the towering ranges were largely leveled. The land lifted. The balmy weather turned cold. Ice sheets scraped across bedrock, pushing a wall of rubble before them. The climate warmed again, and glaciers melted, creating a huge lake that lapped behind the wall of glacial till. Ice sheets kept melting; the lake swelled and stretched and, ultimately, broke through the wall at its lowest part. Rivers began to flow through valleys that the glaciers had carved.

Before politics, culture and high finance, these were the forces that shaped New York City. To see New York thus is to see it with the eyes of a geologist, to see the sweep of millions of years, and to understand why certain things look the way they do and stand where they do. The scar where continents ground together runs down the Bronx River; the remnant of the mountains is the city's bedrock; the rubble pushed by the glaciers gave rise to Long Island; the great lake spilled over at the Verrazano Narrows; the Hudson and East rivers fill valleys deepened by glaciers. Wall Street and Midtown raised modern mountains of glass and granite because there was solid bedrock to build on, but in between lay insufficient foundation for skyscrapers—hence low-slung Greenwich Village and Soho. Before garbage and landfill were strewn in its wetlands,



Manhattan was cut in two when very high tides swelled the rivers and they met each other in the middle of the island, at 125th Street, where a fault slices the city.

All this insight and more can come from a three-hour cruise up the Hudson River—or the East River or through New York Harbor—with Sidney Horenstein of the American Museum of Natural History. “Since geology is the basis of everything, you just cannot help, once you get involved in this, to go beyond the geology,” says Horenstein, author of the

NEW YORK SKYLINE owes everything to geology. The financial district and Midtown support towering buildings because bedrock is no more than 38 to 80 feet below the surface. In Greenwich Village, however, it is about 260 feet down.

Audubon Society's guide to *Familiar Fossils of North America* and coordinator of environmental programs at the museum. “Because if you look at the landscape, you can't help saying, ‘What is that?’ and ‘How did this happen?’”

Horenstein's Circle Line trips, which

for about a decade have taken place in early summer, are as renowned for his observations about geology as they are for his historical anecdotes, questionable puns ("The reason all the lights are lit up here is that we are approaching the Battery") and sayings. On a recent sunset cruise packed with passengers and their picnics, Horenstein explains his answer to the controversial question of how the Big Apple got its name: from a bordello owner named Eve and the "apples" who worked for her. He describes how 300-million-year-old invertebrate fossils ended up in the walls of Riverside Church's bell tower: the sandstone was brought in from Indiana, site of an ancient tropical sea. And a discussion about New York's main rock formations gives Horenstein a chance to quote a favorite refrain: "The Bronx is gneiss, but Manhattan is full of schist. Inwood has lost its marbles, and New York is full of faults."

During other parts of the year, Horenstein gives talks and leads regional geological field trips. "Boats are just one aspect of it," Horenstein says. "I lead tours all over, just like a gypsy cab." One, for example, is a walking tour of Central Park,

where participants can see the scratches carved in schist by roving glaciers and some of the boulders left behind by melting ice. Another lecture series covers geology and travel: how to recognize geologic features wherever you find yourself. (For information about scheduling, check the American Museum of Natural History's Web site at www.amnh.org or call the main reservations line at 212-769-5200.)

Many other paths also wander into New York's geologic past. Charles Mercurian of Hofstra University, author with John E. Sanders of myriad papers on the region's geology, has designed virtual field trips of the city and environs, which can be viewed or ordered at www.duke-labs.com. The Parks Department organizes some excursions as well. And the South Street Seaport Museum's off-site permanent exhibit "New York Unearthed" provides a window into the city's archaeology. For those who want to explore the rocks and faults alone, there is a general site for New York (www.albany.net/~go/newyorker/index.html), with references and materials, as well as several good books, including John Kieran's *A Natural History of New York City and Wild New York*, by Margaret Mittelbach and Michael Crewdson.

If you prefer instead to conjure the

creatures that lumbered through the landscape—to envision the ground sloths, hairy tapirs, saber-toothed tigers, woolly mammoths and mastodons that were the region's wildlife during the Pleistocene—you can find fossil hunters to follow. The New York Paleontological Society, which Horenstein founded in 1970, has monthly meetings most of the year and organizes field trips to look for fossils. One such tour this summer took members to Hamburg, N.Y., to observe Devonian fossils, such as trilobites, in a quarry. Another tour entailed visiting fossil trackways in Connecticut's Dinosaur State Park. (Go to www.nyps.org.)

But no matter which city or state or region or country you are in—or whether you have easy access to a natural history or related museum—you are free to see with a geologist's eyes. Many states have a paleontological society, and although you might have to join to be able to participate in the field trips, membership is typically only about \$20 for a family. A number of states also have a mineral society that leads tours—often these societies are members of the American Federation of Mineralogical Societies (www.amfed.org)—as well as a survey that details the geology of the region. The Utah Geological Survey, for instance, provides local information on dinosaur fossils.

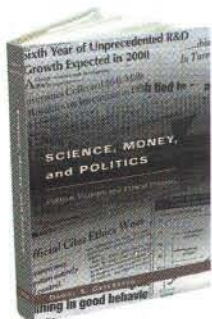
In addition, Horenstein and other experts recommend a helpful series of books. Published by Mountain Press in Missoula, Mont., the *Roadside Geology* books are written by geologists for laypeople (see www.mountainpresspublish.com). Almost half the 50 states have a guide, from *Roadside Geology of Alaska* to *Roadside Geology of Wyoming*. The press also publishes books on various regions of the U.S., several national parks and a few countries, including Canada and Argentina. To see familiar places against the backdrop of aeons is truly a grand view, both humbling and haunting; in the rise and fall of the land in your mind's eye, you can see the earth breathe.

GLACIAL MOVEMENTS left marks on rocks that can be seen in Central Park.



Bloated, Whiny and Self-Important

IS THE SCIENTIFIC BUREAUCRACY THE QUINTESSENTIAL SPECIAL-INTEREST GROUP? BY KEAY DAVIDSON



SCIENCE, MONEY, AND POLITICS: POLITICAL TRIUMPH AND ETHICAL EROSION

by Daniel S. Greenberg
University of Chicago Press, 2001 (\$35)

Dan Greenberg's profoundly important new book depicts American "Big Science" as a classic self-perpetuating bureaucracy—bloated, whiny and self-important. This bureaucracy defends big (and sometimes indefensible) budgets by weaving scare stories about national scientific "illiteracy," questionable "shortages" of scientific personnel, and imaginary threats from foreign competitors. Greenberg quotes an official of the U.S. Office of Management and Budget: "With the possible exception of veterans, farmers, and college students, there is no group that squeals more loudly over a reduction of federal subsidies than scientists. They are the quintessential special interest group, and in effect, they make the oil industry look like a piker."

Startling words? Isn't American science struggling to survive on meager funds, the result of post-cold war budget cuts inspired, in part, by the American people's alleged indifference, even hostility, toward science?

Poppycock, Greenberg replies in a book that is better documented than most National Academy of Sciences reports yet reads as briskly as a Dashiell Hammett detective story. (I devoured it until 4 A.M.) The federal science budget

has gone up, not down, he argues—and presents the statistics to prove it. The American people are not anti-science; in fact, they are very pro-science, almost uncritically so. "By virtually every relevant measure, the United States leads the world in the financing, quality, and volume of research; it has held this lead since the end of World War II, and appears bound to maintain, and increase, its supremacy far into the new century."

So what, Greenberg asks, are scientists griping about? And why do their prime beneficiaries, federal scientific agencies, increasingly act like Madison Avenue hype factories?

"There is too much hype," he quotes Maxine Singer, one of the few female members of the National Academy of Sciences, as saying. "Every gene that is discovered will lead to a cure for cancer. Maybe, but not for a long time. Even the

Superconducting Super Collider was said to have important implications for improving human health."

For anyone naive about the politics of science, *Science, Money, and Politics* is the perfect curative. The military names subs and aircraft carriers after friendly legislators; likewise, federal science bureaucrats affix the names of helpful politicians to their buildings. The National Institutes of Health's "named buildings recognize the good works of senators Warren Magnuson, Lister Hill, Lowell Weicker, Lawton Chiles, and Mark Hatfield, and representatives John Fogarty, William Natcher, Silvio Conte, and Claude D. Pepper."

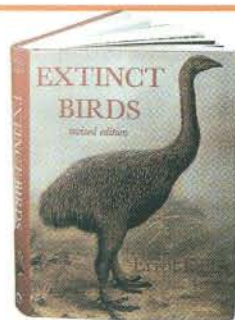
Politics makes strange bedfellows. In the 1980s, as the cold war waned, the U.S. Energy Department, which runs the nuclear weapons complex, feared a major slash in its budget. So it began looking

THE EDITORS RECOMMEND

EXTINCT BIRDS

by Errol Fuller. Revised edition. Comstock Publishing Associates, Cornell University Press, Ithaca, N.Y., 2001 (\$49.95)

"Never send to know for whom the bell tolls; it tolls for thee." John Donne's line, which appears on the dedicatory page, sets the tone for this elegantly written book by British painter Errol Fuller. The author of two other books on birds, Fuller describes here the lives, times and disappearances of more than 80 avian species since 1600. These accounts are illustrated primarily by beautifully reproduced paintings (from a variety of artists, including John James Audubon, J. G. Keulemans and the author) as well as by early photographs and engravings. This revised edition updates the original 1987 publication, reinstating a few birds found not to have disappeared and, sadly, adding a few more that have.



for a new enterprise and found it: the Human Genome Project. Naturally, this upset the NIH, whose officials reasoned that they were more suited to map the genome. But the weapons labs are master lobbyists for their own interests.

President Gerald Ford's science adviser Guy Stever told Greenberg, "I guarantee you, if somebody really had complete control of the quality of our system, and could cut out everything at the low level, we could survive beautifully on less money." In any case, Greenberg says, there is no consistent evidence of a strong correlation between American scientific-technological leadership and the fortunes spent seeking it: "Great Britain has accomplished a great deal scientifically on relatively modest science budgets; the Soviet Union had relatively little to show for its enormous spending on research."

For four decades, Greenberg has been the conscience of American science writers. He was the first news editor of *Science* magazine. In 1967 he established himself as the Jessica Mitford of science when he wrote *The Politics of Pure Science*, an acerbic analysis of science-government relations after World War II. He spent 26 years running the acclaimed gadfly newsletter *Science & Government Report*.

We need more Greenbergs. Too many science writers cover science as uncritically as fashion reporters cover fashion. (I am as guilty of this as many of my peers.) *Science, Money, and Politics* rightly blasts "doting science journalists who faithfully echo the paranoid fears and alarms of the scientific leadership and its publicists." He scolds medical reporters for their "bait-and-switch" coverage of alleged breakthroughs in the war against cancer

and other diseases. Typically, an exciting discovery leads the evening news or is ballooned on the front page. Follow-up research often undermines the claim, but do you see that in the paper? Not likely.

As Greenberg reminds us, science is a big, expensive and all-too-human enterprise, as prone to shams and hucksterism as any human endeavor. Shams and hucksterism are "news," too; they deserve to be covered alongside NASA's latest circus stunts. This admirable book should be required reading for science policy makers, science journalists and any American who gives a damn whenever science—one of the nation's crown jewels—falls into irresponsible hands.

Keay Davidson is a science writer for the San Francisco Chronicle and author of *Carl Sagan: A Life* (John Wiley, 1999).

TIME TRAVEL IN EINSTEIN'S UNIVERSE: THE PHYSICAL POSSIBILITIES OF TRAVEL THROUGH TIME

by J. Richard Gott III. Houghton Mifflin, Boston, 2001 [\$25]

"One reason that time travel is so fascinating is that we have such a great desire to do it," Gott writes. And so he explores the possibilities of travel to the past and to the future. Being a professor of astrophysics at Princeton University, he does not stray from the laws of physics in constructing this stimulating odyssey. Being also the man who has made a number of intriguing predictions based on the Copernican idea that "your location is not special," Gott offers several pre-

dictions here. The future duration of the human species, for one—more than 5,100 years but less than 7.8 million. And because "one of the things we should understand about time is that we have just a little," he argues that "the goal of the human space-flight program should be to increase our survival prospects by colonizing space."



DARK REMEDY: THE IMPACT OF THALIDOMIDE AND ITS REVIVAL AS A VITAL MEDICINE

by Trent Stephens and Rock Brynner. Perseus Publishing, Cambridge, Mass., 2001 [\$26]

Marketed in 1957 as a sedative by Chemie Grünenthal, a German company the authors describe as "notorious for rushing drugs to market with inadequate testing," thalidomide soon launched its ghastly procession of deformed babies. It was removed from the market and appeared to be permanently in limbo. But in 1964 an Israeli physician treating victims of leprosy tried it on a patient with a severe complication of the disease. The patient's condition improved dramati-

cally. Since then, thalidomide has proved effective in treating more than 130 disorders, many of them autoimmune diseases. But because of its menace to reproduction, "everyone involved in the revival of this dark remedy hopes that it will be a short one"—five more years, perhaps—to be followed by a safe analog. Stephens, professor of anatomy and embryology at Idaho State University, and historian Brynner tell this haunting story well.

All the books reviewed are available for purchase through www.sciam.com



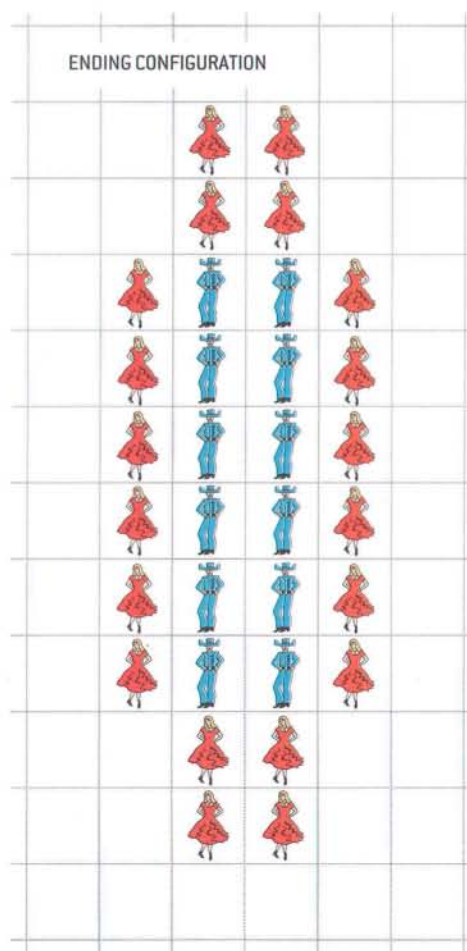
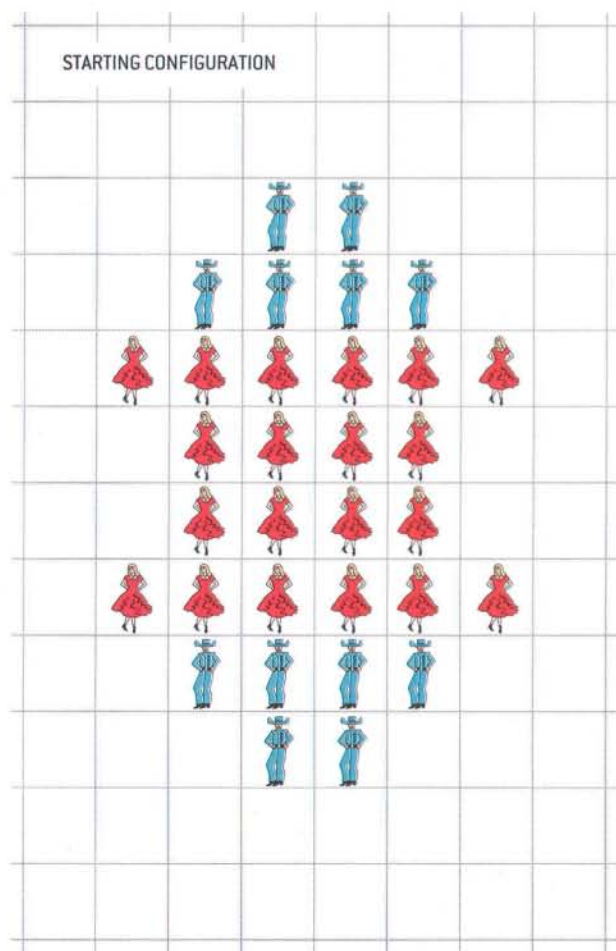
Square Dancing BY DENNIS E. SHASHA

Striding gracefully, her white cape undulating slowly behind her, the director of a famous dance company enters my office. "You've heard of ghost writers," she says. "I need a ghost choreographer." I motion for her to sit, and she outlines the particulars of her problem.

The dance company consists of 12 men (colored blue in the illustrations below) and 20 women (colored red). At a key point in their dance, they go from a configuration in which the men surround the women to one in which the women surround the men. The transition has three stages. During

each stage, each dancer can either stand in place or take one step in one of four directions: to the left, to the right, forward or backward. There are two important conditions: two dancers cannot swap positions during a step, nor can two dancers occupy the same space at the end of a step. Above all, the dancers want to avoid collisions.

The starting and ending configurations of the dancers are shown below. Can you design their moves at each step so that they reach the final position without violating the conditions? It may help to plot the moves on a piece of graph paper.



Answer to Last Month's Puzzle

The solution to the first problem of the unreliable oracle is that you can convert your initial stake of \$100 to at least \$9,309 if you use the optimum betting strategy, which calls for making a first bet of just under \$81.82.

The strategy is fully explained at the Puzzling Adventures page at www.sciam.com. For the second problem, in which you must make all the bets in advance, the best strategy can guarantee you only \$1,600. Again, see the Web site for the full explanation.

Web Solution

For a peek at the answer to this month's problem, visit www.sciam.com



Enter the Dragon Exhibit

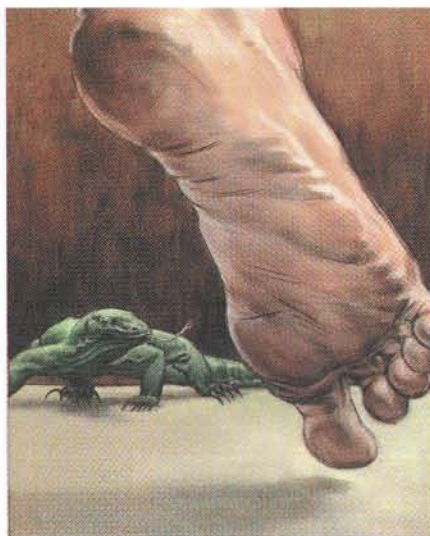
ONCE UPON A TIME THERE WAS A DRAGON AND A BEAUTIFUL PRINCESS, I MEAN ACTRESS, WHO FORGOT THAT LARGE CARNIVORES HAVE A BASIC INSTINCT BY STEVE MIRSKY

Journalists often cite an old bromide: "Dog Bites Man" is not news, but, on the other hand, "Man Bites Dog" is news. And on the other foot, which is exactly where it happened, "Komodo Dragon Bites Newspaper Editor" is definitely news. Especially when the newspaper editor in question is the *San Francisco Chronicle's* semi-celebrity executive editor Phil Bronstein, who was bitten while getting a special up-close-and-perilous tour of the Los Angeles Zoo's Komodo exhibit in early June, arranged for him by his full-celebrity wife, the beautiful actress Sharon Stone. The visit was Stone's idea of an early Father's Day celebration, which often includes dinner out.

Evidently, a zookeeper advised Bronstein to remove his white sneakers so they wouldn't be confused with the dragon's customary meal of white rat. This strategy clearly backfired. A letter to the *Chronicle* asked, "Whose bright idea was it to remove the white shoes from the white feet of a white man in the hopes of not confusing a nearsighted, simpleminded, ravenously hungry lizard?"

I take umbrage at this reader's umbrage, and I feel I am in a unique position to comment on this incident. That position is seated, in front of my computer, far away from any Komodos. For one thing, the Komodo dragon is not merely a lizard. It is "the world's largest living lizard—a ferocious carnivore—found on the steep-sloped island of Komodo in the Lesser Sunda chain of the Indonesian archipelago," according to the hilarious and completely accurate bit by the legendary radio comedians Bob and Ray.

For another thing, the dragon was no doubt well fed, which zoo animals tend to be. As for nearsightedness, Claudio Ciofi of the Zoological Society of London, writing in the March 1999 issue of this magazine, revealed that "monitors [the Komodo is a species of monitor lizard] can see objects as far away as 300 meters, so vision does play a role in hunting, especially as their eyes are better at picking up movement than at discerning stationary objects."



For my final rejoinder to the *Chronicle* reader, I note that Komodos are more single-minded than simpleminded—as an ambush-predator, the Komodo must be cunning and stealthy. And it should probably stay downwind of its prey, what with its amazing body funk. In a lecture, Walter Auffenberg, the world's foremost Komodo expert and author of *The Behavioral Ecology of the Komodo*

Monitor (which, by the way, makes a terrific Father's Day present), remembered the first dragon he met on Komodo: "God, he stank. Oh my goodness. God, he was smelly. I called him Stinky. I went back and told the family that I met Stinky." Auffenberg later learned that Stinky was a "psychotic animal that had probably killed two people on Komodo prior to our visit." Ahhh, good times. (The entire lecture can be found at <http://natzoo.si.edu/hilights/lectures.htm>.)

Anyway, my interest in Komodos was born while working with Ciofi on his article. And even though I learned that the dragons' saliva harbors numerous species of septic bacteria that can kill even if the bite itself doesn't, I was still dumb enough to get next to a Komodo at the National Zoo in Washington, D.C. If you look very closely at the Ciofi story's photo credits, you'll see that I snapped the dragon. (By the way, my visit to the zoo's dragon enclosure was arranged for me by my beautiful actress wife, uh, *Morgan Fairchild*. Yeah, that's the ticket.)

Back in the glamorous world of celebrity maulings, Bronstein underwent surgery to reattach a few tendons, and both his foot and sense of humor seem intact. He told his own paper, "That's how it goes when a movie star and a dragon are involved." Meanwhile Stone's view of the foot-and-mouth business was more Grimm: "Very few women get to see their knight wrestle the dragon. And I think he's kind of fabulous. And kind of hot." With the raging infection that usually follows a Komodo bite, perhaps that heat is just a fever.

Q Why do dogs get blue, not red, eyes in flash photos?

—B. SLOOT, MOUNT PROSPECT, ILL.

Veterinary ophthalmologist J. Phillip Pickett of the Virginia-Maryland College of Veterinary Medicine explains:

"Red eye," the nemesis of amateur photographers, occurs when someone looks directly at the camera while a picture is taken. If the flash is on the same axis as the visual axis of the camera, the reflection off the blood vessels in the person's retina can produce an eerie, satanic look, the so-called red reflex.

Dogs, cats and almost all domestic animals have a special reflective layer in the back of the eye termed the tapetum. Incoming light passes through the animal's retina and is then reflected back through the retina a second time from the tapetal layer. This double stimulation helps these species to see better in dim light. The color of this tapetal layer varies to some extent with an animal's coat color. A black Labrador retriever, for example, will usually have a green tapetal re-

flection. A buff-colored cocker spaniel will generally show a yellow tapetal reflection. Most young puppies and kittens have a blue tapetal reflection until the structures in the back of the eye fully mature at six to eight months of age. "Color dilute" dogs and cats, such as red Siberian huskies and blue point Siamese cats, may have no tapetal pigment and may therefore exhibit a red reflex just like human beings.

Q If a used needle can transmit HIV, why can't a mosquito?

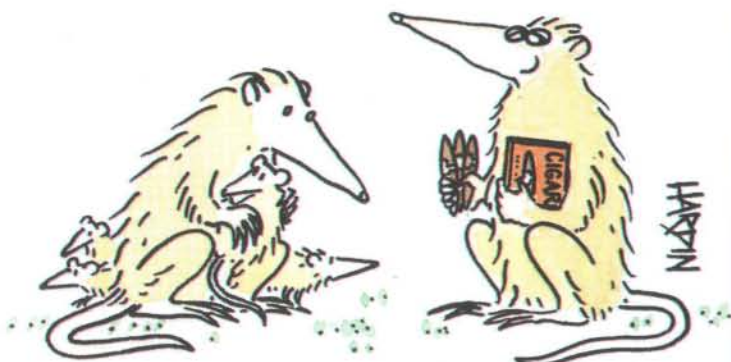
—P. SMITH, MASCLAT, FRANCE

Laurence Corash, chief medical officer of Cerus Corporation, explains:

The AIDS virus (HIV) on used needles is infectious when injected into a human because the virus can bind to T cells and start to replicate. The human T cell is a very specific host cell for HIV. When a mosquito feeds on a person with HIV, the HIV enters the insect's gut, where it cannot find a host.

The malaria parasite, in contrast, can survive, multiply and mature in the mosquito's gut. The parasites then migrate to the insect's salivary glands. Because mosquitoes inject their saliva when they bite, the parasite is passed along to the next human on whom the insect feeds. The complex interaction between the infectious agent and the mosquito is thus required for malaria transmission. HIV, however, deteriorates in the gut before the mosquito bites again and therefore is not transmitted to the insect's next victim.

For the complete text of these and many other answers, visit Ask the Experts (www.sciam.com/askexpert).



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PAPPAL

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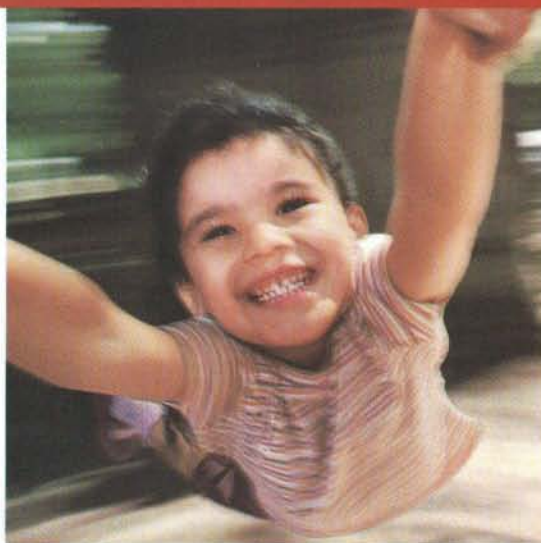
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